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PULMONARY EMBOLISM*

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WHEN I WAS FACED with the question which topic to choose for this presentation, it was clear from the beginning that it should be a subject of broad medical interest and it took me not too long to decide upon *pulmonary embolism*, a problem that has fascinated me for more than 20 years. It is not because I know so much about it, but because this problem is still so full of mysteries, and because we know so little about it, that I wish to consider with you tonight some facets of the complex problem of *pulmonary embolism*.

Last spring at the Boston meeting of the American College of Physicians, Dr. Harold Israel[1] of Philadelphia called pulmonary embolism the most common pulmonary disease in a general hospital. The more than tenfold increase in cases where this diagnosis was made in a leading teaching hospital can only be explained by the greater interest in, and better understanding of, this condition. It has taken a long time, indeed, to develop our present concept of pulmonary embolism and infarction. Since Laënnec first correlated the clinical picture with the pathologic findings which he referred to as "pulmonary apoplexy", the names of many leading pathologists and clinicians, through a century and a half, have been associated with the development of our understanding of pulmonary embolism. The general doctrine of embolism was established by Virchow by experimental and clinical investigations over a ten-year period, 1846 to 1856. Cohnheim, Weigert and Welch clarified the pathogenesis of the hæmorrhagic infarct.

Clinical knowledge and diagnosis have assumed increased importance since the advent of anticoagulant treatment and vein ligation. Since pulmonary embolism is so common and since there is no simple specific test for it, the diagnosis of pulmonary embolism has to be made on clinical evidence which also includes roentgenology. We radiologists are most indebted to Hampton and Castleman (1940).[2] They confirmed the fact that pulmonary infarcts occur most frequently in the lower portion of the lung, less commonly in the midportion, and rarely in the upper portion. They also re-emphasized that the infarct is always applied to a pleural surface; this may be the pleura of the convexity of the lung, at the diaphragmatic and mediastinal surface, or any portion of the interlobar pleura. More clearly than anybody before, Hampton and Castleman demonstrated that the conical or pyramidal shape of the infarct is but a theoretical postulate and that the infarct anatomically corresponds, in fact, to a truncated cone (already recognized by Weigert and Cohnheim about 80 years ago). The apical portion of this cone is usually spared from infarction because of sufficient collateral circulation. The infarcted lower portion of this cone, a hemispherical or cushion-like consolidation, always sits with its longest diameter along a pleural surface.

I shall discuss neither the incidence of embolism or thrombophlebitis, nor Virchow's etiologic triad: (1) slowing of the circulation; (2) intimal damage; (3) increased clotting tendency of the blood. I shall confine my discussion to the question: What can we roentgenologists contribute to the general knowledge and diagnosis of pulmonary embolism?

In a preparation which I owe to Professor Gough in Cardiff, Wales, of a mitral-stenosis lung with marked hæmosiderosis, the first microtome section of the entire left lung shows the brown pigment; in addition, an embolus is present in a medium-sized artery of the lower lobe and there are several fresh and older infarcts. Another section of the same lung, stained with Prussian blue, shows the iron pigment more prominently. There are several infarcts in the lower lobe, truncated cones, with a convex contour towards the hilum.

I should like to present four classical instances of pulmonary infarction.

CASE 1.—A man of 65 had a cholecystectomy for cholelithiasis. On the seventh postoperative day he had chest pain on the left, accompanied by sudden dyspnœa and followed by slight elevation of the temperature to 101° F. The chest film showed some obscurity at the left base, but one could not distinguish whether this was caused by a small pleural effusion or a pulmonary

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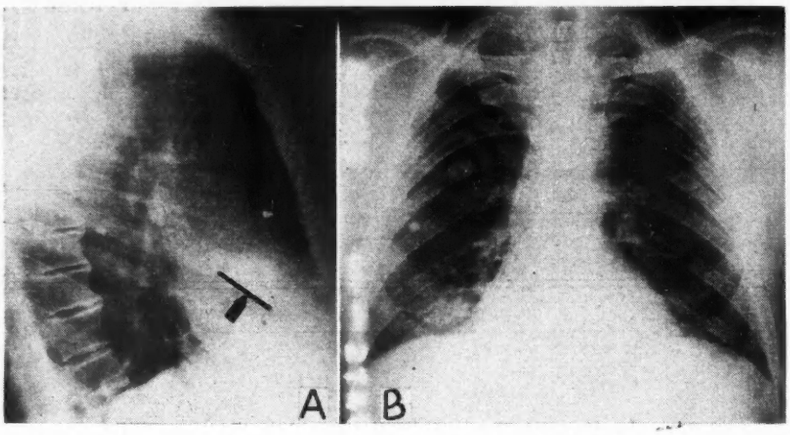

Fig. 1.—Post-traumatic pulmonary infarct. The postero-anterior view shows an ill-defined consolidation in the right lower lung field. The lateral view shows this consolidation in the lower part of the middle lobe with its longest diameter applied to the interlobar pleura (arrow).

consolidation. On fluoroscopy, with proper rotation, a shadow with convex upper contour presented itself in the costophrenic angle—a typical "Hampton's hump"—an infarct. The patient had anticoagulant treatment and recovered.

CASE 2 was that of a truckdriver, aged 54. His classical history, much condensed, tells of a sprained ankle with skin lacerations which kept him in bed for ten days. A thrombophlebitis developed in this leg. After another two weeks he had chest pain accompanied by hæmoptysis. After the third hæmoptysis a chest film revealed an ill-defined consolidation in the right lower lung field and he was hospitalized for operation with the diagnosis of a tumour of the lung. A consolidation of the lateral segment of the middle lobe in broad attachment towards the interlobar pleura was found (Fig. 1). With this history there could hardly be any doubt that this was an infarct. On venography, bilateral extensive thrombosis of the leg veins was found. The patient was treated by bilateral vein ligations and heparin. Last July, after eight years, he came back with a new embolic episode and the old infarct scar.

CASE 3 was that of a 47-year-old man with known mitral stenosis and atrial fibrillation. We saw him during his second episode of pulmonary embolism with infarction. In addition to the multiple infarcts in the right lung, there was a plump, tumour-like hilar shadow. The lung cleared within six weeks; the big hilar artery shadow persisted. Two and one-half years later the patient came back with almost the same findings. This time he succumbed. In the right lung the pathologist found a large, old organized embolus around which the blood had found its way. There was also an occluding fresh embolothrombus with multiple big and small infarcts. The emboli apparently came from a thrombosis in the right atrium. No thrombosis of the leg veins was found. Pulmonary arteriosclerosis of extraordinary degree was ascribed by the pathologist to chronic pulmonary embolism.

CASE 4.—A man of 54 years had thrombophlebitis in the left calf after a long automobile drive and was treated with heparin only for a short time. A week after the treatment had been discontinued he had a severe acute attack of left abdominal pain. He was readmitted with the diagnosis of "acute abdomen" and the suspicion of a perforated viscus. An ill-defined obscurity at the left lung base was found. Four days later the presence of a pulmonary infarct was established (Fig. 2). While the heparin treatment was reinstituted, the thrombophlebitis flared up. I have included this case to illustrate that one has to look for the significant topographic relation of an otherwise non-characteristic consolidation. The routine posteroanterior or lateral view may incidentally reveal this relation to the pleura. But only by careful fluoroscopy may we be able to establish this relation for an apparently nondescript consolidation seemingly centrally located.

We see here another less common feature of infarcts, those linear extensions; they are accompanying areas of atelectasis. When an infarct shrinks to a flat, subpleural, barely visible, fibrotic plaque, these lines, sometimes converging, may be the only recognizable residue pointing to the infarct scar. Similar lines have been mistaken for infarcts though they represent atelectatic plates often in the absence of infarcts.

We have just discussed four instances of pulmonary embolism with infarcts: one occurring after

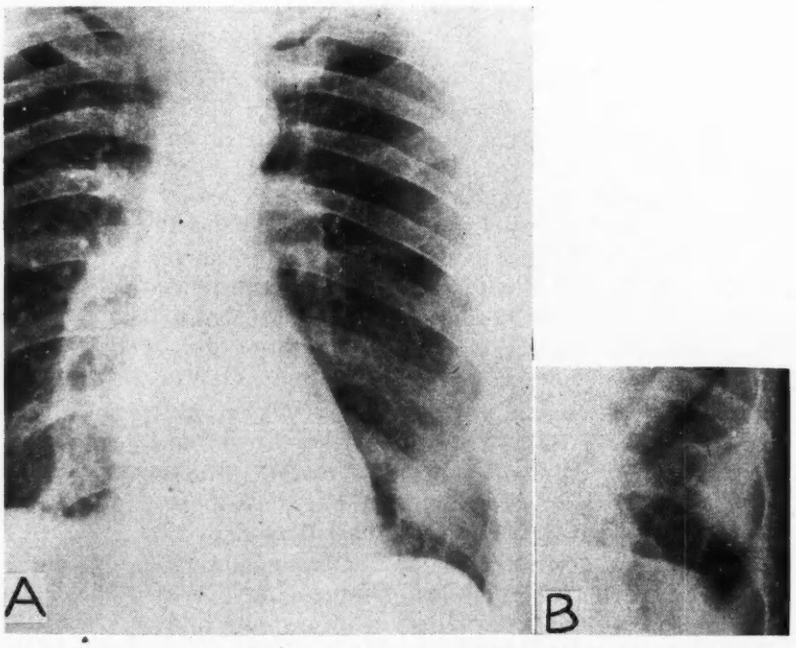

Fig. 2.—Pulmonary infarct in the left lower lobe. In the postero-anterior view an ill-defined, apparently central consolidation is seen at the left base. The spot film taken under fluoroscopic positioning shows the half-spherical consolidation applied to the chest wall in the posterior axillary region. Plate-atelectatic areas extend from the infarct as linear shadows into the adjacent lung.

an abdominal operation, the second after a leg trauma with prolonged bed rest, a third in mitral stenosis with thrombi in the right heart, and another in a middle-aged man as a complication of thrombophlebitis induced by prolonged sitting in the driver's seat. We are reminded of the "shelter deaths" during the blitz over London in 1940.

Fig. 3.—Diagram demonstrating common features of pulmonary infarcts. The characteristic arrangement along the pleura must often be searched for by proper positioning.

The diagram (Fig. 3) summarizes this chapter of our story, namely the classical roentgen appearance of a small or medium-sized infarct. On the right we see several infarcts presenting themselves in profile view in proper relation to the pleura: towards the chest wall, in the costophrenic angle, in the cardiophrenic angle, or towards the pleura of the horizontal fissure. On the left they form ill-defined nondescript shadows, and we need a lateral or oblique view to throw them into proper profile and position. Practically any shadow in the chest roentgenogram may be cast by an infarct. An infarct may even occupy a full middle lobe or the greater portion of the lower lobe, but this is rare. This well-defined silhouette is not present from the first moment. It usually takes one or two days for an ill-defined cloudiness to condense to this better defined consolidation. The question is sometimes asked: How soon can one see an infarct roentgenologically? In the moment when it develops. How soon after the embolization does an infarct develop? It varies; sometimes within a few hours, often after a few days; in many instances no infarct develops at all, as we shall discuss in more detail presently.

Here is the occasion to mention another fact. One great difficulty which we radiologists had to overcome was the belief that every infarct goes necessarily through all the stages of congestion, extravasation, necrosis, demarcation and cicatrization, although the experimental pathologists had shown that the process may stop with extravasation. How often in the past were we disappointed to see a consolidation disappear in a few days or weeks when we had felt certain that we were dealing with an infarct, from the roentgenologic appearance and the clinical constellation. "Again," we thought in disappointment, "our diagnosis was apparently wrong". And it took us a long time to learn the lesson. Hampton and Castleman coined the term "incomplete and reversible infarction". This is commonplace now, but was revolutionary only 17 years ago.

Thus, any consolidation in the lower and mid lung fields in proper relation to the pleura may represent an infarct. That it is an infarct must be proven by the history, symptoms, other roentgen or clinical signs, including electrocardiogram and vectorcardiogram, the exclusion of other possibilities, or the further course. But one must not demand a complete set of arbitrarily chosen signs, before the diagnosis is accepted. For example, hæmoptysis is reported in a certain series only once out of six cases of embolism. If one waited for hæmoptysis, one would miss the diagnosis in five of them.

At this point I would like to present this statistical table condensed and simplified from autopsy data of Hampton and Castleman.[2]

STATISTICAL DATA ON 370 CASES OF PULMONARY EMBOLISM AND INFARCTION

Postoperative	40% of which 58% had infarcts
Cardiac medical	30% of which 90% had infarcts
Noncardiac medical	30% of which 62% had infarcts

From this we learn the numerical relation—in a given series—between surgical and medical patients; the medical cases prevail also in the series of other authors. The formation of infarcts, too, shows a distinct distribution. In cardiac patients embolism almost always causes infarcts. In noncardiac medical patients, including many elderly, debilitated subjects with chronic, often malignant disease and prolonged bed rest, about two out of three develop an infarct if they are overcome by pulmonary embolism. Contrarily, among the surgical patients, who comprise also many younger subjects with an intact cardiovascular system, hardly more than one out of two patients with embolism form infarcts.

These are figures collected on patients who died —the severe cases, those where the total resistance and the cardiovascular apparatus broke down. This is—to use the terminology of statistics—not a representative sample of the universe. This is a highly biased sample, obviously distorting the over-all picture in favour of infarct formation. But even here, the instances of pulmonary embolism without infarct are not rare. There is convincing clinical evidence that *pulmonary embolism without infarct* formation is still much more common among survivors.

Recognizing that in many instances of embolism no infarct develops, or sometimes develops only later in the course of the disease, we have asked ourselves in which way the radiologist can help the clinician in the diagnosis of pulmonary embolism, in the absence of infarct formation.

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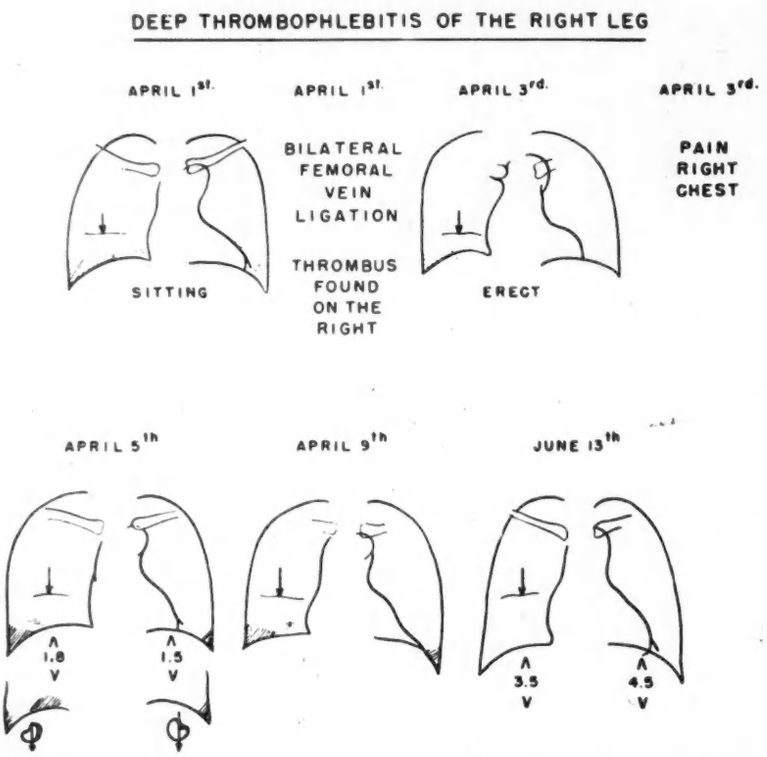

Fig. 4.—Respiratory inhibition as early evidence of pulmonary embolism. The infarcts were identified later in the course of the disease. Complete recovery from the ventilatory inhibition.

A. Dyspnœa, tachypnœa and chest pain are listed as leading signs and symptoms of pulmonary embolism. We are here not concerned with experimental evidence or the theories whether respiratory difficulties are caused by voluntary or reflex splinting, by bronchospasm, or by vagal, sympathetic or chemical depression of the respiratory centre. Respiratory inhibition, general or unilateral, is a clinical fact in many, if not most instances of pulmonary embolism.

In a diagrammatic synopsis of the clinico-roentgenologic observations on a 68-year-old woman (Fig. 4), we notice the onset of pulmonary embolism by the high position of both sides of the diaphragm, and the diminished distance from the right dome of the diaphragm to the horizontal interlobar fissure, a reliable sign of poor aeration of the right middle and lower lobes. A thrombus was found at femoral vein ligation. A short time later we could identify three infarcts. The respiratory excursion slowly recovered and the lung was normal two months later.

In some of these instances we may see inhibited ventilation with basal atelectasis where infarcts are manifest from the beginning, or appear later, or do not appear at all. Diminished ventilatory excursion and reduced aeration, if not accounted for otherwise, are suggestive of pulmonary embolism.[3, 4]

B. Pulmonary embolism, mostly with infarcts, may cause *pleural effusion*. Thus, a unilateral or bilateral pleural effusion may be correctly diagnosed as such, yet the underlying cause not recognized. The exclusion of tuberculosis, congestive heart failure and malignant tumour together with positive evidence in the form of a sudden painful onset, blood on thoracocentesis, respiratory inhibition, dyspnœa or acute cor pulmonale may help to make the correct diagnosis in an early stage. We have found a certain combination of roentgen signs quite diagnostic: High position of both sides of the diaphragm, ill-defined obscurity of both bases, probably caused by basal atelectasis and small pleural effusions, short interlobar-diaphragmatic distance, evidence of acute pulmonary hypertension (to be discussed presently) with the clinical picture of a "chest cold", a viral infection or sometimes an "acute surgical abdomen"—this usually turns out to be pulmonary embolism.

In the last few years we have learned more about acute cor pulmonale. You are familiar with the observations first made by McGinn and White (1935).[5] In many instances of pulmonary embolism an extra load is placed upon the right ventricle owing to acutely increased pulmonary vascular resistance. This condition may be diagnosed by certain auscultatory, electrocardiographic, and vectorcardiographic findings. It is believed that there are no roentgen signs in acute cor pulmonale, as there are no anatomic findings in the heart itself at postmortem. If we concentrate, however, on the concept of acute pulmonary hypertension we will find valid suggestive roentgen evidence in numerous instances.

Before we proceed to these roentgen findings let us consider an extraordinary observation. This case was published under the title "Pulmonary Infarction Mistaken for Bronchogenic Carcinoma". I wish to acknowledge our gratitude to the authors, Parkins and Bradshaw,[6] for their frank admission of a diagnostic mistake and the unique detailed report.

A 56-year-old man with a six-day history of chest pain, cough and hæmoptysis, had a consolidation of the lateral segment of the middle lobe and an ovoid mass corresponding to the lower hilar shadow on the right. He was operated on with the presumptive diagnosis of bronchial carcinoma. The involved segment of the middle lobe was resected. The pulmonary artery at the right hilum presented an aneurysm-like pulsating dilatation corresponding to the hilar mass seen on the roentgenogram. A needle aspiration from it produced blood. The patient survived the operation but succumbed to an embolic episode two days later. The essential data are as follows: The patient had thrombosis of the deep veins of the right calf. He experienced an embolic episode with an infarct in the right middle

lobe. The old emboli and infarction were identified by the pathologist. At the time of operation he was still in the stage of acute cor pulmonale or acute pulmonary hypertension. Peripheral arteriospasm caused increased vaso-resistance and caused also the aneurysmal dilatation of the main branches of the pulmonary artery on both sides. After death—without any arterial pressure—the arterial tree was collapsed, as you would expect, and no aneurysmal dilatation was seen by the pathologist.

This is a unique observation: the classical constellation of thrombo-embolic disease with a recent episode of embolism, inspection in the open chest of the dilated hilar arteries in acute pulmonary hypertension, and proof during life and at autopsy that there was no big embolo-thrombus lodged there.

Extensive studies in mitral stenosis have shown that vasoconstriction may be an important factor in producing pulmonary hypertension. The success of the surgical treatment of mitral stenosis depends a good deal on the reversibility of this marked elevation of pulmonary arterial resistance, which therefore is functional to a certain degree and caused by vasoconstriction. Returning to our subject of pulmonary embolism, Westermark[7] has described a lack of blood filling of a lobe or one lung in pulmonary embolism. Furthermore, the plump, tumour-like hilar shadow is another sign recognized in recent years. Hanelin and Eyler[8] have analyzed cases of massive chronic and subacute pulmonary embolism with large embolothrombi lodged in the hilar arteries. They demonstrated convincingly that these large thrombotic masses may form the core of the plump hilar shadows, as in our Case 3. Thus pulmonary artery obstruction may play a direct part in the causation of the roentgen signs of oligæmia (increased radiance) of the lung field and the plump hilar shadows. However, experimental data and clinicopathological correlation suggest that functional phenomena involving the pulmonary vasculature, i.e. reflexes originating from arteries lodging emboli, come into play too. These pathophysiologic phenomena, reminding one of Wood's[9] vasoconstrictive pulmonary hypertension, do not permit a close roentgen-pathologic correlation, just as the acute cor pulmonale syndrome itself lacks a morphologic counterpart on the necropsy table. In the endeavour to recognize pulmonary embolism in those numerous instances without gross infarction, we have learned to rely on functional roentgen signs of cardiovascular nature. It is assumed that the embolic insult incites spastic contraction of medium-sized and small pulmonary arteries and arterioles, thus increasing vascular resistance. The right ventricle pumps harder, overcoming this increased resistance, the arterial pressure rises and the big hilar branches (of relatively poorer muscular equipment, "elastic" rather than "muscular" arteries) dilate under this increased pressure. Thus, this arteriospasm and not solely mechanical blocking by the emboli causes the extraordinary increase in pulmonary resistance and the extra load on the right ventricle.[4]

A few illustrations: A 26-year-old man was admitted to the hospital on June 8, 1955, for stabbing pain in the right chest and a small hæmoptysis occurring that morning. Two days later a small consolidation was seen on the right (Fig. 5). Five days after the onset, the roentgen diagnosis of pulmonary infarct was definite.

Heparin treatment was started. The width of the right hilar artery increased from 11 mm. on June 8 to 14 on June 13 and 22 mm. on June 20, with return to 15 mm. on August 31. At the same time the right lung field was oligæmic except for the area of infarction. At the height of the pulmonary hypertension on June 20, with a hilar artery diameter of 22 mm. the pulmonary artery trunk also showed considerable dilatation. He had another embolic episode with infarction a few days later and recovered after bilateral femoral vein ligation and continued anticoagulant treatment.

We see here the transient morphologic constituents of acute cor pulmonale: spasm of the peripheral pulmonary arteries causing obligæmia of the lung fields, and pulmonary hypertension causing dilatation of the central arteries.

A similar sequence of events occurred in the case of a 34-year-old woman with pulmonary embolism during the puerperium. The right hilar artery increased from 15 mm. to 17 mm., then diminished to 13 mm. and 12 mm. in width. Roentgenograms showed the appearing infarct and a small atelectatic plate left behind for a short time, as well as ventilatory inhibition and oligæmia of the lung field.

This wealth of roentgen signs of pulmonary embolism and acute cor pulmonale is not always present, of course, in this completeness. If episodes of embolism are repeated over months or years, or if particles of thrombotic masses lodged in the central pulmonary arteries are showered into peripheral vessels over a long period of time, permanent vascular changes are established, the vascular resistance is permanently increased and cor pulmonale of the low-output or high-resistance type develops, as described by Cournand.[10]

The man whose roentgenograms are shown in Fig. 6 was observed with repeated episodes of pulmonary infarction for about seven years. The two roentgenograms in Fig. 6 are 3½ years apart, 1947 and 1950. There were already changes in both hilar vessels on the earlier film. Nevertheless, you see on the left the arterial branches extending downward. And on the later roentgenogram after three embolic episodes in between, the tail of the left hilar shadow is amputated, the lung is oligæmic, and the pulmonary artery trunk shows a convex bulge where there was a smooth concavity on the earlier roentgenogram; also signs of right ventricular dilatation have become evident. This chronic cor pulmonale developed under our eyes from repeated embolic episodes. This history was confirmed by the pathological findings a year later.

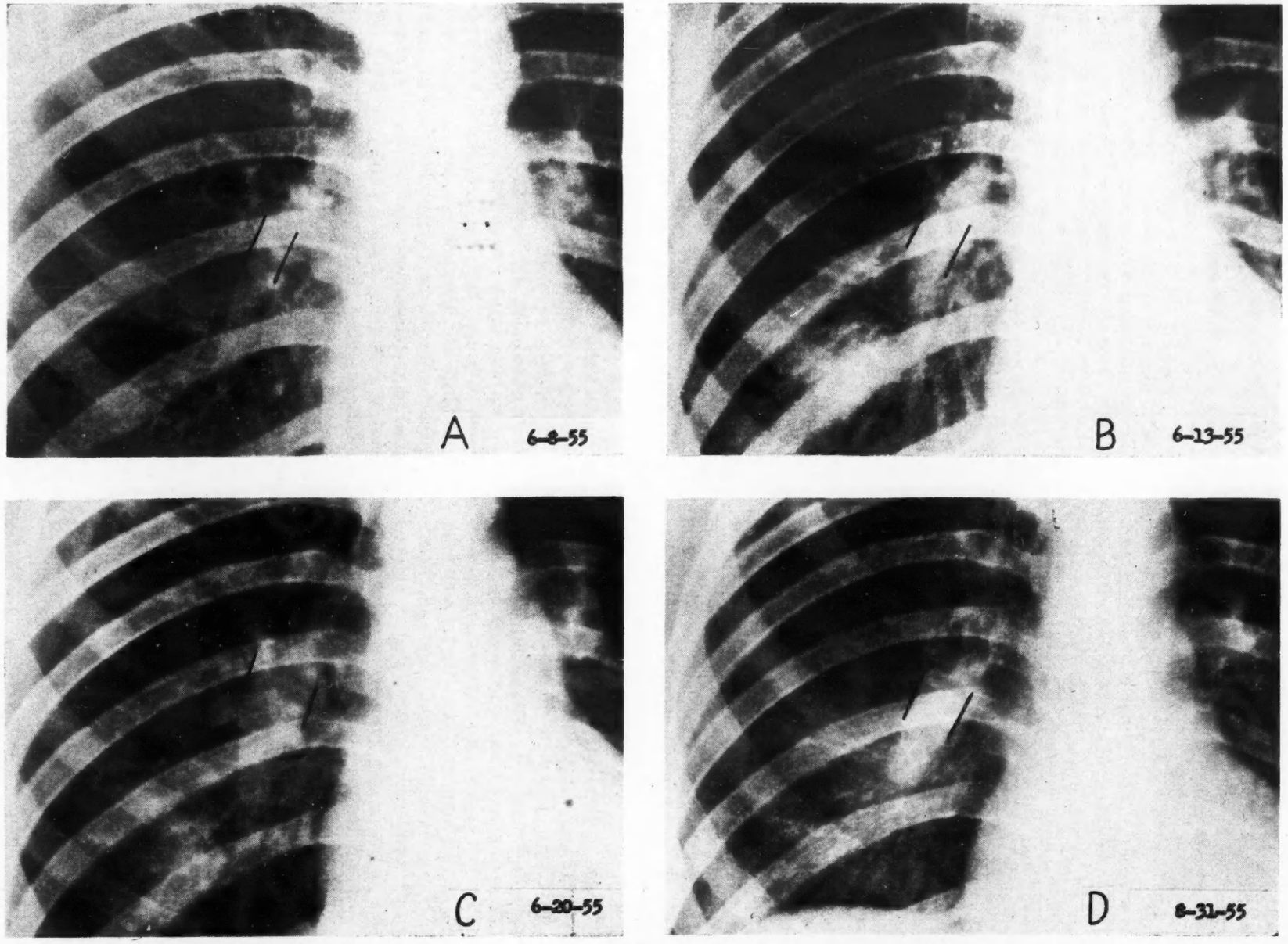

Fig. 5.—An episode of pulmonary embolism with infarct and acute cor pulmonale. The right hilar artery trunk on June 8, 13 and 20 measures 11, 14, and 22 mm. respectively, to return to 15 mm. on August 31. Oligæmia of the lung field is most marked on B and D. At the height of the episode of pulmonary hypertension the pulmonary artery trunk is markedly dilated, D.

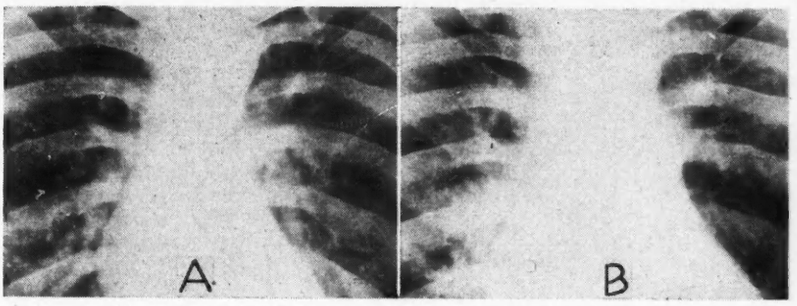

Fig. 6.—"Amputation" of the tail of the left hilar shadow and oligæmia of the left lower lung field developing during 3½ years in a patient with recurrent pulmonary embolism. Noticeable development of chronic cor pulmonale with dilatation of the pulmonary artery.

Four years ago, Owen and his associates[11] of the Massachusetts General Hospital published a study of 12 cases of cor pulmonale caused by unrecognized chronic pulmonary embolism. The following is a case to the point.

This patient used to be an active manager in a department store. She was seized by sudden severe dyspnœa which incapacitated her within a few weeks so that she had to give up her job. This happened at the age of 44 years. We saw her 16 months later, in June 1952, and at that time she had already all signs and symptoms of chronic cor pulmonale. We observed her through two more years with seven hospital admissions and numerous visits to our out-patient department. There was a loud P^2; a systolic murmur and thrill in the pulmonic area; by electrocardiogram and vectorcardiogram, right ventricular hypertrophy. Roentgenograms showed marked right ventricular dilatation, and marked dilatation of the pulmonary artery which became aneurysmal in the later stages; plump dilatation of the hilar arteries and oligæmia of the peripheral lung fields, the classical cor pulmonale of the high-resistance type. On catheterization by Dr. L. Dexter, it was found that the pulmonary arterial pressure was 71/37 mm. Hg with a mean of 35 mm. Hg. There was no evidence of a shunt. A short time before she died in right heart failure, we observed for the first time small infarcts at the right base. From the sudden onset of the illness, however, and the episodic, almost paroxysmal progress, the diagnosis of chronic pulmonary embolism and chronic cor pulmonale had been made long before.

The pathologist (Dr. L. Reiner) found extreme hypertrophy and dilatation of the right ventricle. The weight of the right ventricle, in relation to that of the left, was about four times the normal. There was severe atheromatosis in the pulmonary artery stem and main branches. Many old and fresh embolothrombi were present in the smaller arteries. The findings were similar to those recently shown by Dr. Castleman in a Cabot case,[12] presenting in medium-sized arteries masses of fibrotic tissue, which were weblike and adherent, others forming bridges "reminding one of mucosa bridging in ulcerative colitis" (Castleman).

It is our opinion—and we share it with others—that numerous, probably most cases of so-called primary or idiopathic pulmonary hypertension are of this chronic, embolic etiology.[13] Certainly, it is often impossible to distinguish these two entities during life and very difficult even at necropsy.[14, 15] The practical implication of substituting a known morbid process which you can treat for an unknown, needs no further explanation.

This subject of pulmonary embolism is inexhaustible, of course. I have not even mentioned septic infarction and the differential diagnosis in general. Let me close my discussion with the hint that the question is not always "Is it one of two or three possibilities? Is it myocardial infarction or pulmonary infarction?" Sometimes it is both. In several series of patients who died after recent myocardial infarction, thromboembolism was a coexistent contributory cause of death in 6 to 15%.

We had known the man of 59 years, whose roentgenograms are shown in Fig. 7, for some time. We saw him last in the summer of 1955, recovering from a myocardial infarction with congestive failure. He came back three months later with a new myocardial infarct and two pulmonary infarcts, one in the upper portion of the middle lobe, as if suspended from the interlobar fissure. The recurrent myocardial infarct and the pulmonary infarcts were confirmed 10 days later by necropsy.

SUMMARY

1. Pulmonary embolism is common, in medical cases with and without cardiovascular disease, after operations and injuries, during pregnancy and the puerperium.

2. As long as we have not learned how to prevent pulmonary embolism, the early diagnosis is important in order to protect the patient against further embolic episodes.

3. The complete classical clinical symptomatology is the exception. Pulmonary embolism may simulate any kind of cardiac, pulmonary, pleural, neurologic, or acute abdominal disease.

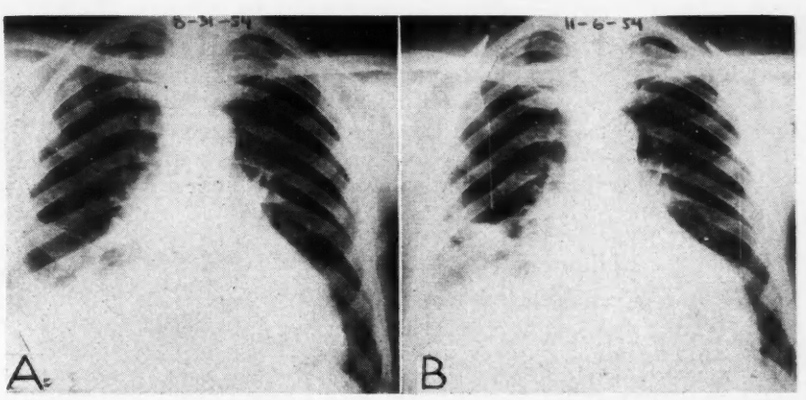

Fig. 7.—Pulmonary infarct in the upper portion of the middle lobe occurring with recurrent myocardial infarction. A. The patient had just recovered from acute myocardial infarction. Residual pleural effusion. B. About two months later: recurrent myocardial infarction and pulmonary infarcts.

4. Among the signs and symptoms, chest pain and dyspnœa, singly or combined, are the most common early signals. Hæmoptysis is comparatively rare.

5. If pulmonary infarction is diagnosed by clinical means or roentgenologically, this signifies that there has been an episode of embolism.

6. The "triangular shadow" of the infarct is a fiction. Consolidations of any shape may be caused by infarcts. The classical appearance is a consolidation of cushion or hemispherical shape, with its longest extension arranged along a pleural surface. This may be the lateral, diaphragmatic, mediastinal or any interlobar pleura. The exact relation to the pleura must be elicited, in many instances, by proper positioning under fluoroscopy. Most infarcts are located in the lower portions of the lung, fewer in the mid-lung field, and only rarely do they occur in the upper lung field.

7. Incomplete infarction, i.e., blood extravasation without necrosis and eventual scar formation, is apparently more common than the classical infarct.

8. Many instances of embolism, probably the majority, occur without infarct formation.

9. Roentgenologically, in addition to the classical infarct, we look for signs of impaired ventilation, such as high position of the diaphragm, diminished ventilatory diaphragmatic excursion and basal atelectasis, often in the form of plate atelectasis. The diminished distance between the right dome of the diaphragm and the horizontal interlobar fissure is a good yardstick for inhibited ventilation. This ventilatory inhibition may occur on one side only or bilaterally.

10. Pleural effusion may be the first objective clinical and roentgenologic manifestation of pulmonary embolism. The effusion may hide an infarct which becomes visible with resorption, or after thoracocentesis with evacuation of the fluid. Sometimes the infarct is minute and not detectable roentgenologically.

11. The syndromes of acute and chronic cor pulmonale or pulmonary hypertension are often revealed by: (a) dilated hilar arteries forming a plump tumour-like hilar shadow; (b) dilatation of the pulmonary artery trunk, most common in chronic embolism; (c) increased translucency due to oligæmia of the lung field—lobar or unilateral in acute embolism, unilateral or bilateral, more often in chronic embolism; (d) dilatation of the right ventricle in chronic cor pulmonale, best recognized by the increased area of contact between heart and anterior chest wall in the lateral roentgenogram; (e) right inflow stasis as manifested by dilatation of the azygos vein and superior vena cava.

I am fully aware that we have not solved tonight the mysteries of thromboembolic disease. I shall be content, however, if I have stimulated your renewed interest in these perplexing problems and if I have possibly helped to clarify our thinking in one or the other respect. Finally, I hope that I was able to show that the roentgenologist can often lend valuable help in these rather common, and often critical clinical situations.

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RÉSUMÉ

L'embolie pulmonaire est une complication fréquente des affections médicales avec ou sans atteinte cardiovasculaire, des opérations et des blessures, de la grossesse et du puerpérium. Comme nous n'avons pas encore trouvé le moyen de prévenir l'embolie, il importe d'en faire le diagnostic précoce afin d'en éviter la répétition. Le tableau clinique classique ne se rencontre que rarement; au contraire l'embolie pulmonaire peut imiter toutes sortes de lésions, cardiaques, pulmonaires, pleurales, neurologiques, ou un abdomen aigu. La douleur thoracique et la dyspnée, ensemble ou isolément, sont les avertissements les plus fréquents. L'hémoptysie est plutôt rare. Si l'on établit un diagnostic d'infarctus par la clinique ou la radiologie on peut supposer l'embolie préalable.

L'opacité triangulaire classique par laquelle on décrivait l'infarctus ne correspond pas à la réalité: les consolidations des foyers infarcis peuvent prendre n'importe quelle forme. L'apparence typique, s'il en est, serait plutôt celle d'un cône tronqué dont la base est en apposition avec la plèvre (latérale, diaphragmatique, médiastinale ou interlobulaire). La relation précise avec la plèvre ne peut quelquefois n'être découverte qu'à la fluoroscopie. La plus grand nombre d'infarctus se trouve dans la portion inférieure du poumon, quelques-uns se logent dans la portion moyenne et très peu dans la portion supérieure. L'infarcissement incomplet, c'est-à-dire l'extravasation sanguine sans nécrose ni cicatrice, se produirait plus souvent que l'infarctus classique. La majorité des embolies, probablement, se produit sans causer d'infarctus.

En radiologie, en plus de l'image déja décrit, on recherche les signes de gêne ventilatoire comme l'élévation du diaphragme et la diminution de ses mouvements ainsi que l'atélectasie basale, souvent d'apparence laminée. La diminution de la distance entre la voûte de droite du diaphragme et la fissure interlobaire horizontale donne un bon aperçu de cette gêne ventilatoire qui peut impliquer les deux côtés ou un seul. L'épanchement pleural peut être la première manifestation objective clinique et radiologique de l'embolie pulmonaire. Cet épanchement peut masquer un infarctus qui ne devient visible qu'après sa résorption ou son évacuation par thoracentèse. Quelquefois l'infarctus est minuscule et peut échapper à l'examen radiologique. Le syndrome de la souffrance aiguë ou chronique du cœur droit, ou de l'hypertension pulmonaire comprend: la dilatation des artères hilaires offrant l'apparence d'une ombre tumorale siégeant au niveau du hile; la dilatation du tronc de l'artère pulmonaire, surtout dans l'embolie chronique; une plage pulmonaire plus translucide à cause de l'oligémie, unilatérale ou lobaire dans l'embolie aiguë, plus souvent bilatérale dans l'embolie chronique; la dilatation du ventricule droit dans le cœur pulmonaire chronique, mise en évidence par l'augmentation de la surface de contact entre le cœur et la paroi thoracique antérieure dans les clichés latéraux et enfin la stase du retour veineux se manifestant par une dilatation de la veine azygos et de la veine cave supérieure.

REDUCED RAILWAY FARES

Arrangements have been completed with the Canadian Passenger Association to permit members and their families to obtain reduced railway fares in travelling to and from the meetings of the C.M.A. and/or affiliated medical societies in Halifax, N.S., and St. Andrews, N.B., next June. For details see page 635 of the issue of April 15.

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ECHO 9 VIRUS INFECTIONS IN EASTERN CANADA: CLINICAL AND LABORATORY STUDIES

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Introduction

Research on virus meningitis or so-called aseptic meningitis has revealed that a range of viruses possessing different biological properties may be involved. Thus Coxsackie viruses B1, B2, B3, B4 and A9, as well as Echo viruses types 6 and 9, have been isolated from cerebrospinal fluid and stools. Coxsackie A7 virus has been recovered from stools and Echo virus type 4 from stools and throat washings. More recently, attention has centred round the isolation of Echo types 6 and 9 viruses from widespread epidemics of aseptic meningitis occurring in England, Continental Europe, and North America. In the majority of instances primary isolation has been accomplished in monkey kidney cell cultures, but a few viruses have been isolated on human amnion, HeLa cells and infant mice.

A review of world literature indicates that Echo viruses 6 and 9 are frequently responsible for virus meningitis and that four other varieties, namely, types 2, 4, 5 and 14, may cause a lesser proportion. Echo 6 virus has been recovered from the stools, cerebrospinal fluid and throat washings of patients studied in the U.S.A. and in England. Karzon *et al.* (1956)[20] and Davis and Melnick (1956)[9] isolated virus in monkey kidney tissue cultures and propagated it serially in this medium. More recently Echo 9 viruses have been recovered from cases of aseptic meningitis, both with and without rash, by a number of workers situated over an extensive geographical area. Rotem (1957)[34] reported the presence of infection at Leicestershire in England. Boissard *et al.* (1957)[2] described cases from East Suffolk, and Hennessen (1956)[17] did likewise from Sauerland in Germany. Cases due to Echo 9 infection have also been reported from Belgium by Nihoul *et al.* (1957).[29] Further cases of aseptic meningitis have been associated with Echo 4 virus, and Lehan *et al.* (1957)[23] have reported such cases from Marshall County, Iowa, where the disease described was thought to be etiologically related to the virus isolated. The clinical significance of certain recent findings has been discussed by Blattner (1958).[1] For the convenience of the reader, Table I contains a list of pathogenic viruses isolated from cases of aseptic meningitis.

Our studies during the period March to September 1957 showed that a widespread epidemic occurred in Nova Scotia and Newfoundland and also affected New Brunswick and Prince Edward Island.

The purpose of the present publication is threefold: (a) to present a clinical description of Echo 9 virus infections observed during an outbreak of aseptic meningitis; (b) to draw attention to the use of human amnion cells as a convenient and readily available medium for the isolation of this agent; (c) to report the pathogenicity of strains recovered to suckling mice.

Symptoms and Signs

Forty patients from whom Echo 9 virus was isolated were studied clinically; 33 of these were under 15 years of age, 27 were male and 13 female. Of the females, two were in the first trimester of pregnancy and one was in the second.

The onset in most cases was insidious but a few patients gave a clear-cut history of a 24-hour period of complete remission early in the disease. The course of the illness was variable, being most severe in young adults and teen-agers.

Headache, nausea and vomiting were the outstanding symptoms and were present in all patients old enough to state their complaints. Other common complaints were stiff neck, feverishness and muscle pains. A rash was seen in 10 of the patients studied. This was maculopapular, pink, and distributed chiefly on the face, neck and trunk. The lesions varied in size from 1 to 3 mm. in diameter and were present from 24 to 48 hours. Less frequent complaints were chills, dizziness, photophobia and constipation.

Physical findings in most cases were few and consisted of a moderate elevation of temperature and stiffness of the neck. Spasm of the hamstrings and the presence of Kernig's sign were noted in about 25% of cases. The deep reflexes were normal and there was no evidence of cranial nerve palsies. Muscle tenderness was present in two patients who represented the most severely ill members of the series. One was a youth of 14, the other a man of 50; both presented with severe throbbing frontal and occipital headache, photophobia, nausea and vomiting, and pain and stiffness of the neck, back and limbs. Their disease was clinically indistinguishable from severe pre-paralytic poliomyelitis. In contrast to this, there were three young children in a small localized epidemic who had no complaints whatsoever. The average duration of illness in the series was nine days and there were no complications or unfavourable sequelæ.

The average of 26 white blood cell counts was 9500 per c.mm. (only two were over 15,000). A cerebrospinal fluid (C.S.F.) pleocytosis featuring mononuclear cells was seen in nearly all cases. The average of 35 determinations was 389, with a high of 2240 and a low of 8. The C.S.F. chloride levels

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TABLE I.—Viruses Isolated from Cases of Aseptic Meningitis

Virus	*Source*	*Medium*	*Country*	*References*
Coxsackie	Stools	Suckling mice	U.S.A.	Dalldorf and Sickles 1948[7]
				Dalldorf *et al.* 1949[8]
				Dalldorf 1949[6]
	Stools	Suckling mice	U.S.A.	Curnen *et al.* 1949[5]
A7	Stools	Monkeys (live)	Russia	Chumakov, M. A. and Voroshilova, M. K. (cited by Habel and Loomis 1957[15])
A9	CSF	Monkey kidney	U.S.A.	Melnick 1957[24]
B1-4	CSF	?	U.S.A.	Hummeler 1957[18]
B2	Stools, T. wash.			
	CSF	HeLa		
		Suckling mice	U.S.A.	Hummeler *et al.* 1954[19]
B2	Serum, stools	Suckling mice		
		Monkey kidney	U.S.A.	Shelokov and Habel 1957[37]
B2, 4	Stools and CSF	Suckling mice		
		Monkey kidney	Canada	Rhodes and Beale 1957[33]
				Duncan *et al.* 1955[10]
B5	Stools, T. wash.	Liver and œsophagus		
		HeLa, M. kidney	U.S.A.	Syverton *et al.* 1957[38]
Echo 2, 3, 4, 5, 6 and 14	Stools	Monkey kidney	World wide, definition and report	Committee 1955[4]
Echo 2	?	?	U.S.A.	Melnick 1957[24]
4	Stools, T. wash.	Monkey kidney	U.S.A.	Lehan *et al.* 1957[23]
				Chin *et al.* 1957[3]
5	CSF	?	?	Melnick 1957[25]
6	Stools, T. wash.			
	CSF	Monkey kidney	U.S.A.	Karzon *et al.* 1956[20]
7	?	?	U.S.A.	Melnick 1957[24]
9	Stools, T. wash.	Monkey kidney	Germany	Hennessen 1956[17]
				Odenthal and Wunder 1956[30]
9	Stools, CSF	Monkey kidney	Belgium	Nihoul *et al.* 1957[29]
9	Stools, CSF	Monkey kidney and human amnion	Canada	Laforest *et al.* 1957[22]
9	Stools	Monkey kidney and human amnion	England	MacLean and Melnick 1957[26]
9	Stools, CSF			
	T. washings	Monkey kidney	England	Boissard *et al.* 1957[2]
9	Stools, CSF	Monkey kidney		
		Monkey testes		
		Human amnion	W. Europe	Quersin-Thiry *et al.* 1957[31]
9	Stools, CSF			
	T. washings	?	England	Rotem 1957[34]
9	Stools, CSF	Monkey kidney	Canada	Faulkner *et al.* 1957[12]
14	CSF	?	U.S.A.	Melnick 1957[25]

were normal or very nearly so in all cases; protein level was normal or slightly elevated, with an average of 41 mg. % in 29 determinations.

Table II contains a summary of Echo 9 virus isolations in Eastern Canada.

Virus Studies

Pathological specimens received included cerebrospinal fluid, throat washings, stools and anal swabs. Host cells used for isolation were, for the greater part, monkey kidney since this has been considered the cell of choice for Echo viruses (Sabin, 1957).[35] Earlier attempts to grow this virus in human amnion were unsuccessful (Faulkner *et al.*, 1957),[12] but continued efforts revealed that the virus was cultivable. All cultures were incubated at 37° C. in a stationary position, 5 degrees from the horizontal. Culture fluid was changed as required, but in most cases cytopathogenic effect (CPE) was evident (in 2 to 3 days) before fluid changing was necessary.

Cerebrospinal fluid (0.5 ml.) was inoculated into the washed cells, incubated for one hour at 37° C., and 1.0 ml. maintenance medium added. Throat washings were ground with alundum powder, centrifuged, and penicillin and streptomycin added to the supernate; the method of culture was the same as for cerebrospinal fluid. Stools were prepared following the method of Kibrick *et al.* (1955),[21] a 10% suspension being used as inoculum. Anal swabs were placed, when collected, directly into a buffered saline solution which was used as the inoculum (the swab was vigorously agitated in the fluid to release as much virus as possible). Virus isolations were obtained from all four types of specimen.

Amnion cell cultures. The first report of the growth of cells of full-term human amnion and their use comparable to monkey kidney cells for propagation of polio virus is considered to be that of Zitcer *et al.* (1955).[42] Weinstein *et al.* (1956)[39] subsequently published their method of trypsinization of amnion and its use for the growth of polio virus and some of the Coxsackie viruses. Many other reports followed. The method in use in this laboratory is a modification of that originally developed by Enders (1956)[11] and incorporates certain procedures recommended by Wilt *et al.* (1956).[40]

Immediately upon receipt, placenta is suspended by the cord from a bar and the amnion stripped by blunt dissection. The amniotic membrane, after thorough washing (six or seven times) in phosphate buffered saline (PBS) containing 500 units of penicillin and 500 micrograms of streptomycin per ml., is cut into pieces of about 2 to 3 sq. cm. These pieces are placed in an

TABLE II.—Summary of ECHO 9 Isolations in Eastern Canada from March to September 1957

Patient	*Age*	*Sex*	*Doctor*	*Locality*
Ash, W.	6	M	J. W. Davies	St. John's Fever Hospital, Nfld.
Bal, A.	7	M	K. Smith	Spryfield, N.S.
Bar, M.	30	F	J. W. Davies	St. John's, Nfld.
Bas, Wm.	7	M	Joan Crosby	Protestant Orphan's Home, Halifax
Bea, A.	11	M	H. L. Stewart	Halifax, N.S.
Bur, S.	4	F	S. Nathanson	New Waterford, N.S.
Car. K.	½	F	A. J. Campbell	Halifax, N.S.
Cor. M.	4	M	Helen Hunter	Halifax, N.S.
Cre, J.	11	M	Joan Crosby	Protestant Orphan's Home, Halifax
Dou, D.	24	F	K. Smith	Spryfield, N.S.
Dou, Y.	24	F	H. L. Knodell	Halifax, N.S.
Dow, S.	20	F	J. W. Davies	St. John's Fever Hospital, Nfld.
Duf, S.	11	F	Joan Crosby	Protestant Orphan's Home, Halifax
Gal, D.	½	M	J. A. Delahunt	Halifax, N.S.
Gar, N.	10	M	R. Ritchie	Halifax, N.S.
God, B.	1	M	M. E. Burnstein	Halifax, N.S.
Har, R.	5	M	M. Munnich	Fairview, N.S.
Har, M.	10	M	H. Ross	Halifax, N.S.
Hel, M.A.	3	F	Joan Crosby	Protestant Orphan's Home, Halifax
Hel, E.	6	F	Joan Crosby	Protestant Orphan's Home, Halifax
Lam, R.	4	M	G. Pace	Dartmouth, N.S.
Mil, D.	11	F	J. W. Davies	St. John's, Nfld.
McL, D.	4	M	D. MacKeigan	Dartmouth, N.S.
McN, B.	6	M	Joan Crosby	Protestant Orphan's Home, Halifax
Ram, G.	25	F	A. Gordon	Eastern Passage, N.S.
Ree, B.	10	M	A. M. Creighton	Tatamagouche, N.S.
Sac, C.	14	M	R. McInnis	Enfield, N.S.
Sac, D.	11	M	R. McInnis	Enfield, N.S.
Sci, Y.	31	F	I. A. Bowie and J. E. MacDonnell	Port Hood, N.S.
Smi, B.	6	M	Helen Hunter	Halifax, N.S.
Smi, G.	9	M	Helen Hunter	Halifax, N.S.
Tib, G.	14	M	P. Jardine	East Chezzetcook, N.S.
War, D.	5	F	U. Weste	Tufts Cove, N.S.
Wea, D.	6	M	Joan Crosby	Protestant Orphan's Home, Halifax
Why, K.	5	M	Joan Crosby	Protestant Orphan's Home, Halifax
Wil, O.	4	M	R. Langley	Spryfield, N.S.
Woo, G.	4	M	U. Weste	Woodside, N.S.
Cla, F.	10	M	J. W. Davies	St. John's Fever Hospital, Nfld.
McD, S.	50	M	C. A. Gordon	Halifax, N.S.
Tho, L.	½	F	R. McInnis	Enfield, N.S.

Erlenmeyer flask, 100 ml. of growth media is added, and the whole is incubated overnight at 28° C. The following morning the fluid is removed and discarded, the tissue fragments are placed in a Rappaport flask, and 200 ml. warmed trypsin is added (0.25% solution of 1:250 Difco trypsin in Hanks (1949)[16] balanced salt solution, with pH adjusted to 7.8). The contents of the flask are gently agitated by a magnetic stirrer henceforth. Predigestion is carried out for 30 minutes, and the supernatant fluid then discarded. Fresh trypsin is added and thereafter continuous-flow trypsinization at 37° C. carried out; the amount of trypsin entering the flask and the cell suspension leaving the flask is kept at a constant level, such that in a period of 2½ hours one litre of trypsin flows through the system; the cell suspension is collected in a flask kept in an ice bath. Two ml. of hyaluronidase (300 turbidity-reducing units equivalent to 1000 viscosity units) is added to the suspension, which is then filtered through one layer of gauze into chilled 250-ml. centrifuge cups and centrifuged at 1000 r.p.m. for 15 minutes. The deposit is washed with Scherer's (1953)[36] maintenance solution (M.S.), again centrifuged, and the supernate discarded. The cells are made up to a 1:100 volume with growth medium and stored at 28° C. overnight. In the morning they are subjected to a second cycle of centrifugation (1000 r.p.m. for 15 minutes), the cells resuspended in growth medium to the same volume and counted. The volume is adjusted to give a concentration of 300,000 cells per ml. and the suspension dispensed into 16 x 125 mm. screw-cap tubes, each tube receiving 1 ml.

The medium used for growth of cells is one composed of Scherer's maintenance solution (M.S.) 60%, human serum 10%, horse serum 10%, glutamine 10% and tryptose phosphate broth 10%. Before use for virus propagation the cells are washed three times in Scherer's M.S. to remove all traces of human serum. After infection, the maintenance medium consists of Scherer's M.S. 80%, horse serum 10% and tryptose phosphate broth 10%.

Monkey kidney.—Monolayer monkey kidney cell cultures (Youngner, 1954)[41] are prepared using the continuous trypsinization technique of Rappaport (1956).[32] Originally the medium used for growth consisted of a synthetic medium, No. 202 (Franklin 1956),[13] and human serum, while that for maintenance was No. 202 alone. Since other workers were obtaining good results following the inclusion of tryptose phosphate broth in media for HeLa and amnion cells (Ginsberg *et al.*, 1955,[14] and Wilt *et al.*, 1956),[40] it was decided to incorporate it in our media for a trial run; the results were satisfactory and maintenance for a longer period without degeneration was possible. Growth and maintenance media in current use are as follows: for growth, medium No. 202, 85% plus tryptose phosphate broth, 10% plus human serum, 5% is employed. For maintenance, medium No. 202, 95%, plus tryptose phosphate broth 5% is used. Before inoculation the cells are washed three times in No. 202 medium.

Virus isolations.—From a group of 141 cases clinically designated as aseptic meningitis, we recovered a range of cytopathogenic agents in monkey kidney and human amnion tissues. These were serologically identified as Coxsackie A9 and B4; poliomyelitis viruses Types II and III; and Echo 9 virus. For the purpose of the present study we have selected only those 40 strains of virus which have been serologically neutralized in high titre by specific Echo 9 antiserum; 19 of these were obtained in primary culture from either stool or C.S.F. material on human amnion cells. Of 40 such strains, 38 were pathogenic to suckling mice.

Susceptibility of Infant Mice

All of our strains, in the form of 0.02 ml. of tissue culture passage fluid, were inoculated intraperitoneally into 24-hour-old Swiss white mice. Mice were randomized and one or more families of eight were inoculated with each strain. Altogether 70 families, consisting of approximately 600 mice, were used. During the course of mouse pathogenicity tests, no mice infected with any other virus were housed on the premises. Pregnant mice were obtained at periodic intervals and the health of the animal colony was good. Inoculated mice developed symptoms of illness after incubation periods ranging from 4 to 11 days, the average being 6 days. Of the isolates, 38 caused clinical illness together with histological changes in the skeletal muscles. The incidence of illness in the stricken families was 65%. The disease tends to be progressive and is characterized by the following changes. Activity is decreased, often with generalized tremor. The mice become dehydrated and of a pale grey hue. Respiration becomes rapid.

Extension and paralysis of the hind legs develop and the animals attempt to crawl with the aid of their forelegs, but there is some retention of ability to flex the hip joint. Eventually, complete flaccid paralysis of all limbs develops, followed by wasting, respiratory failure and death.

The histological changes were found by post-mortem examination on representative mice with clinical illness resulting from the inoculation of the above 38 strains. Postmortems were also performed on two litters each inoculated with monkey kidney tissue culture material and non-inoculated. The following tissues were removed and examined histologically—brain, heart, fat pad, pancreas, liver, skeletal muscle from limbs and thoraces. These were fixed in 5% formalin solution for 48 hours and then stained with the standard hæmatoxylin and eosin stains used routinely in the Pathological Laboratory. Selected sections were stained with phosphotungstic acid hæmatoxylin and periodic acid Schiff stains. No histological changes were found in any organs except the skeletal muscles of animals inoculated with tissue culture materials which showed the presence of cytopathogenic agent. The following changes are seen in the skeletal muscles: lack of uniformity of muscle fibres with early hyalinization, swelling and œdema; paleness and loss of cross striations; infiltration with inflammatory cells—mostly mononuclears, with intense proliferation of primitive mesenchymal cells; fragmentation and destruction of fibres and appearance of empty sarcolemma sheaths.

Discussion

A series of 141 cases of aseptic meningitis observed in the Atlantic Provinces have been subjected to clinical and virological studies. From two patients we recovered Coxsackie A9 virus, from one patient Coxsackie B4 virus, from three patients poliomyelitis virus. From 36 patients unidentified agents were obtained. From 40 cases Echo 9 virus was obtained, and thus clinical and laboratory accounts of Echo 9 infection form the text of the present publication.

In considering the clinical syndrome of Echo 9 infection, a variety of interesting possibilities worthy of further investigation arise. Thus, many of our cases could have passed unnoticed as examples of severe headache, save for the fact that the attention of local clinicians had been focused on the disease and a search for cases was conducted. The frequency with which isolation of virus was possible from the C.S.F. has emphasized the value of virological examination of the latter in all cases of severe headache of idiopathic character.

The relationship of Echo 9 disease with rash to rubella is worthy of future scrutiny. The lack of a suitable laboratory test for rubella virus has proved a major handicap to the accurate identification of rubella. The rash observed in Echo 9 virus infection bears a close similarity to that of rubella and it is not improbable that the two conditions could have been confused in the past. But whether or not the two diseases are identical etiologically remains open to conjecture, and further research alone can decide. It should also be mentioned that the conditions designated roseola infantum and Boston exanthem (Neva and Enders 1954,[27] Neva and Zuffante, 1957)[28] merit similar consideration. It is hoped that the continued efforts of clinical and laboratory personnel will help to establish etiological diagnoses for some of the exanthemata and fevers of unknown origin so frequently encountered in medical practice. In view of the correlation between rubella and congenital deformities, we believe that a search for Echo 9 virus should be conducted in the pregnant female in the event of any patient developing such signs and symptoms as we have described in association with Echo 9 virus infection.

The growth of Echo 9 virus in tissue cultures of human amnion provides a convenient and perhaps more readily available laboratory medium for recovery of the agent than monkey kidney tissue. From three pregnant women, we isolated Echo 9 virus in primary culture on human amnion cells, but it is also interesting to record that pregnancies continued uninterrupted to date. The growth of Echo 9 virus in human amnion at present would appear to be of academic importance, but the existence of Echo 9 virus amnionitis during pregnancy is a possibility which should not be ignored.

Observations on the pathogenicity of Echo 9 virus to suckling mice, originally reported by Boissard *et al.* (1957),[2] have been confirmed and extended by us. Histological changes seen in the skeletal muscles of infant mice bear the closest resemblance to those first described by Dalldorf and Sickles (1948).[7] These are pathognomonic of Coxsackie A virus infection and manifest clinically as herpangina of the infant, but the counterpart of this disease in the adult is obscure. Another apparent difference seems to be that whereas Dalldorf and Sickles were able to induce changes in suckling mice by direct inoculation of fæcal materials, the authors and others have only succeeded in doing so by injection of monkey kidney or human amnion culture material.

Conclusions

Echo 9 virus has been isolated from 40 cases of aseptic meningitis which have been studied clinically.

Headache, nausea and vomiting, stiffness of the neck, feverishness and muscle pains were prominent symptoms. Moderate fever, nuchal rigidity and normal reflexes were cardinal physical findings.

A maculopapular rash was noted in some 25% of our cases.

A C.S.F.-pleocytosis featuring mononuclear cells was a constant finding.

Virus was readily isolated from C.S.F., stools and throat washings on monkey kidney and human amnion cells in primary culture.

The viruses isolated were antigenically similar, serologically typed as Echo 9 virus, and shown to be pathogenic to infant mice.

Some implications of our findings are discussed in relation to the etiology of severe headache, roseola infantum and rubella.

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RÉSUMÉ

En abordant ce travail nos lecteurs voudront sans doute se reporter à un article antérieur paru dans ces pages (livraison du premier septembre 1957) sur le même sujet. Les auteurs se sont rendu compte depuis lors, qu'une véritable épidémie de méningite aseptique s'était abattue sur les provinces maritimes pendant l'été '57. Des 141 cas qui furent vus au cours de ces quelques mois, on réussit à isoler le virus Echo 9 chez 40 malades. Le tableau clinique comprenait de la céphalée, des nausées, des vomissements, de la fièvre, des courbatures et de la raideur de la nuque. Dans 25% des cas on observa une éruption maculopapulaire, rosée, intéressant la face, le cou et le tronc.

Le liquide céphalo-rachidien présentait une pléocytose. Dans plusieurs cas l'affection simulait à s'y méprendre la phase préparalytique de la poliomyélite. Les auteurs soupçonnent, qu'il existe une relation entre cette infection et la rubéole, la roséole et l'exanthème dit de Boston. Ils recommandent que des recherches plus poussées soient faites dans ce sens.

ABDOMINAL PAIN OF CEREBRAL ORIGIN IN CHILDREN*

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SOME CONFUSION and divergence of opinion is present in the current medical literature, concerning the subject of abdominal pain of cerebral origin in children. For instance, Wallis[1] in a recent monograph gives a number of examples of children who had paroxysmal abdominal pain, often associated with headache or vomiting, and commonly with a family history of migraine, who he states are all examples of "masked epilepsy". Apley and Lloyd[2] compared the electroencephalograms of 133 children with recurrent abdominal pain but no demonstrable organic disease with a control group and found essentially no difference between them. They came to the conclusion that there is no relationship between epilepsy and recurrent abdominal pain in children. Farquhar[3] reviews a group of 112 children with paroxysmal symptoms of abdominal pain or headache or vomiting. He formed the opinion that migraine was the etiological factor for the abdominal pain in all his cases. Reimann[4] ascribes a similar clinical picture to a disease entity which he calls "periodic disease", the true nature of which is uncertain. He does say, however, that migraine is a fairly common accompaniment both in the patient and his family. The cases seen recently at The Hospital for Sick Children, Toronto, were reviewed in an attempt to resolve some of the difficulties associated with their diagnosis.

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MATERIAL

The criteria used for selection of cases were as follows:

1. The presenting complaint should be abdominal pain.
2. There should be no local cause for the pain.
3. The pain should not consistently be the aura of a generalized seizure.

There were 19 such cases in the group. Ages of patients ranged from two to 13 years.

CLINICAL FEATURES

The attacks themselves fell into two fairly clear-cut clinical types.

Type I.—There were 17 cases in this group. Typically, the child will be outside, playing normally, when he stops, comes into the house, complains of abdominal pain and wants to lie down. The mother notices that he is pale. He may complain of headache and often has some nausea. He may vomit. The pain is periumbilical or epigastric. It is usually not "crampy" but may be severe enough to make the younger children cry. The child becomes drowsy and may fall asleep. The duration of the attack is variable but usually ranges between one hour and six hours, and in exceptional cases it may continue intermittently for 48 hours. In most instances, if the child falls asleep, he is symptom-free when he wakes.

Type II.—There were two cases in this group. In each the episode was shorter and the pain tended to be more severe. The onset was abrupt and consisted of epigastric or periumbilical pain and pallor. At the same time the patient became confused and wanted to lie down. The episode was over in five to ten minutes but was followed by drowsiness. In one of the two cases this episode had been immediately followed by a generalized seizure on several occasions. In the great majority of occasions, however, the epigastric pain, pallor and confusion had occurred alone.

Age.—The age of the patients when first seen ranged from two to 13 years with a mean of seven years. The age of onset of attacks ranged from two years to 11 years, with a mean of four years. On several occasions, the parents gave information which suggested that similar symptoms might have been present before this. For instance, one parent said that at the age of one month the child began to have episodes in which she went pale, grunted and appeared to have abdominal pain. The whole affair lasted for about five minutes. The majority of children, however, began having their attacks between the age of two and five years.

Family history.—One of the most striking things about the clinical picture is the family history. Thirteen children had parents or siblings of parents with migraine. Of the other six, one had similar attacks as a child, one sibling had centrencephalic epilepsy, and in four no significant family history was obtainable.

Of the children presenting with attacks of Type I, 13 (75%) had a family history of migraine. Neither of the two children in Type II had a family history of migraine.

Examination and special tests.—In no case was there a demonstrable abnormality on physical examination, and with the exception of the electroencephalogram special investigations were also normal.

The electroencephalograms were of interest. They were not done in two cases. They were normal in eleven cases. In three cases there was a minor slow wave dysrhythmia with no focal or unduly paroxysmal features. In two instances there were frequent fast spike discharges from the right temporal region. In one instance there was a burst of bilaterally synchronous atypical spike and wave with no cortical localization. If these electroencephalograms are correlated with the clinical picture, it is seen that the patients who have the longer type of attack—Type I—have all the normal electroencephalograms, the three electroencephalograms with the mild dysrhythmia and the single example of atypical spike and wave. The two children who had the brief attacks—Type II—had spike discharges in their temporal regions.

In summary of the clinical findings, one can say that these children seem to present in two distinct ways. In the first and commonest the attack lasts an hour or longer and may be accompanied by pallor, headache, nausea or vomiting. The child will usually be drowsy and will sometimes fall asleep. Upon wakening he is usually normal. There is a family history of migraine in the majority of cases. The electroencephalogram is normal or shows a mild, generalized dysrhythmia. In the second and smaller group the attacks are characteristically much shorter—five to ten minutes only. They consist of a sudden onset of abdominal pain, some confusion and pallor. The attack is often followed by drowsiness. The electroencephalogram shows a focal abnormality in the temporal region, and a family history of migraine is uncommon.

DISCUSSION

At this point an attempt must be made to define the conditions of migraine and epilepsy. In this paper the very simple stand is taken that migraine is primarily a disturbance of blood vessels producing secondary changes in the brain, whereas epilepsy is caused by primary discharges in the brain. The clinical differences between true migraine and epilepsy have been reviewed many times and are well known. The most important differentiating point is discussed by Sir William Gowers,[5] who points out in his monograph "The Borderland of Epilepsy" that in migraine the onset of sensory phenomena is gradual and progresses over a period of many minutes or longer; in epilepsy the symptoms are characteristically abrupt and if there is an extension it takes place over a period of seconds.

Thus the first group of cases I would prefer to call "abdominal migraine" for want of a better word. The second group it would seem is true "abdominal epilepsy".

In many respects the attacks are very similar. The cerebral site is probably identical and lies in the region of the insula. It is the mechanism of production of the abnormal cerebral function that is different in the two groups.

The single example of a child who had long attacks and atypical spike and wave patterns in the electroencephalogram is difficult to classify. She had a strong family history of both epilepsy and migraine. She had two quite distinct forms of attack. In one she had occasional major convulsions with no localizing features and no aura. In the other she had attacks of umbilical abdominal pain which would last up to two hours and would come on at any time of the day for no apparent reason. On no occasion was the umbilical pain followed by a generalized seizure and there seemed to be no relation between the two events. One is tempted to assume that this child had the two separate abnormalities of centrencephalic epilepsy and abdominal migraine rather than that the abdominal pain was a manifestation of the same seizure discharges which caused her convulsions.

The treatment of abdominal epilepsy is the same as the treatment of any other kind of epilepsy. It consists essentially of anticonvulsant medication and, in rare instances, cortical excision. In the treatment of abdominal migraine drug therapy plays but a small part. In the longer attacks Cafergot (caffeine and ergotamine) can occasionally inhibit the episode if it is given at the onset. In some instances small continuous doses of phenobarbitone or diphenylhydantoin (Dilantin) are of value. In most cases the attacks continue in spite of medication. The most important facet of treatment is reassurance of the child and his parents. It is well known that these attacks are made more frequent by anxiety and tension. A fundamental of treatment is to have the parents understand that the child should lead a normal life and that the episodes, whilst tiresome, are benign. A diagnosis of epilepsy is, even in this relatively well informed age, hardly conducive to this point of view.

As an example of how important it is to establish the correct etiological factor in the management of the patient, this case history is of interest:

A girl, aged six years, presented with a three-year history of paroxysmal attacks of abdominal pain lasting several hours and associated in some instances with nausea and vomiting. Laparotomy and appendicectomy had been performed on two separate occasions because of the pain. There was a strong family history of migraine. Subsequently an electroencephalogram was taken which showed diffuse slow activity, a diagnosis of "abdominal epilepsy" had been made and she was treated with maximum doses of anticonvulsant medication. This diagnosis had caused acute anxiety in the parents, with consequent increase of their already over-protective attitude towards the child. The medication had produced some drowsiness and confusion in the child in spite of which the symptoms had progressed and the attacks were occurring very frequently. With a large amount of reassurance and a reduction in medication, clinical improvement was very considerable and she rapidly returned to leading a relatively normal life although still having occasional attacks.

SUMMARY

Nineteen children with abdominal pain of presumed cerebral origin were studied. It was found that they could be divided into two clinical groups. The first, and much the commoner, was characterized by attacks lasting an hour or more and often associated with vasomotor disturbances, nausea, vomiting or headache. Drowsiness was common during the attack. There was a family history of migraine in the majority of children and the electroencephalograms were normal or showed a mild generalized dysrhythmia. It is suggested that these children are examples of abdominal migraine.

The second group is characterized by attacks lasting five or ten minutes and associated in some instances with confusion, vasomotor disturbances, nausea or vomiting. A family history of migraine is not characteristic and the electroencephalogram shows evidence of discharges in the temporal region. It is felt that these are examples of true abdominal epilepsy.

From a therapeutic point of view it is a mistake to call the first group "epilepsy" because the anxiety so engendered in the family group tends to make attacks more frequent.

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RÉSUMÉ

Dix neuf enfants accusant des douleurs abdominales que l'on croyait d'origine cérébrale, furent observés à l'Hôpital des enfants malades de Toronto. On se rendit compte que ces petits malades pouvaient se partager en deux groupes: le plus nombreux des deux comprenait ceux dont les accès de douleur duraient une heure ou plus et s'accompagnaient de troubles vaso-moteurs, nausées, vomissements et céphalées. La somnolence se manifestait souvent au cours de ces crises. Ces enfants possédaient des antécédents familiaux de migraine et l'électroencéphalogramme habituellement normale pouvait quelquefois montrer des anomalies discrètes généralisées. L'on suggère que ces enfants soient considérés comme des cas de migraine abdominale.

L'autre groupe était caractérisé pas des attaques d'une durée plus brève (cinq ou dix minutes) accompagnées dans certains cas d'obnubilation, de troubles vaso-moteurs, de nausées et de vomissements. Les antécédents familiaux de migraine étaient rares sinon absents et l'E.E.G. montrait un foyer d'activité anormale dans la région temporale. Ceux-ci semblent être des exemples de véritable épilepsie abdominale.

Au point de vue thérapeutique, il importe de distinguer les deux groupes car un diagnostic d'épilepsie posé chez un individu du premier groupe peut engendrer une telle angoisse dans le milieu familial du sujet qu'il contribue à aggraver les attaques.

OBSERVATIONS ON THE IN VIVO DISTRIBUTION OF RADIOIODINE IN THYROID DISEASE*

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D. L. WILANSKY, M.D., F.R.C.P.[C.],
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INTRODUCTION

RADIOACTIVE IODINE (I^{131}) has a well-established place in the study of thyroid disease. For example, the uptake of radioiodine by the thyroid gland is a more direct quantitative test of thyroid function than is basal metabolic rate or serum cholesterol, both of which are subject to more extrathyroidal variables. Yet the uptake test is only one of several tests of value in this regard. On the other hand, for evaluating the function of different parts of the thyroid gland, or of thyroid tissue occurring outside the neck, measurement of the selective uptake of radioiodine by the tissues in question constitutes the only method available at the present time. The technique of determining the distribution of I^{131} *in vivo*, variously referred to as scanning, mapping, scintiscanning or scintography,[1, 2] is now in use by many endocrine clinics in North America and Europe.

Certain limitations of the method as it is now used must be borne in mind during evaluation of results. Firstly, only gross distributions of the radioisotope may be determined and it cannot give the precise information provided by autoradiography of a histological specimen. Secondly, it can give no indication of the chemical form in which the radioisotope occurs in the tissues. Thirdly, the map is a two-dimensional projection of the three-dimensional distribution of the isotope in the gland; consequently, variations in concentration in depth will not be shown. Thus in some instances it may not be possible to determine whether radioiodine is present in a nodule or in tissue anterior or posterior to the nodule.

Despite these limitations, useful information can be obtained with this technique. It is the purpose of this paper to draw attention to those thyroid disorders about which the method may offer information of practical value.

METHOD

Scanning is usually carried out 24-48 hours after ingestion of a tracer dose of radioiodine. At this time most of the radioiodine remaining in the body has been concentrated in the thyroid gland. It has been our practice to carry out the procedure 24 hours after oral administration of 40-50 μc. of I^{131}.

With the patient in the supine position, the neck is surveyed with a detector sensitive to the gamma rays emitted by the radioiodine. While the detector and its housing may take on a variety of sizes and shapes, ours is representative of most in use at the present time. The detector consists of a thallium activated sodium iodide crystal, 1 inch (2.5 cm.) in diameter and 1 inch long, in conjunction with a photomultiplier tube. These units along with some associated electronic circuitry are enclosed in a brass cylinder. In addition, the crystal is surrounded by lead shielding and a conically shaped lead shield is affixed in front of the crystal. The latter is 3 inches in length and has a central hole down the axis of the cone ⅜ inch in diameter. A set of three cylindrical lead inserts, each with a different diameter hole, may be placed into this cavity, so that the diameter of the central hole actually used may be chosen to suit the circumstances. Such inserts are called collimators and render the detector highly directional. A flashlight bulb is situated at the centre of the face of the crystal so that a beam of the light may be directed down the collimator. This is very useful since it provides a marker on the skin indicating the region which lies within the field of view of the detector.

A complete scan is carried out as follows. The detector is set over the neck to the extreme left or right, at or just below the level of the suprasternal notch, with the tip of the collimator about ⅜ inch above the skin. The detector is driven across the neck at a uniform rate by a motor drive. Upon reaching the other side of the neck, the detector is advanced a short distance cephalad and a second traversal is made by reversing the direction of the drive. Successive traversals are made in this fashion until the presence of the chin renders further scanning impossible.*

The output of the scanning unit is coupled to a scaler, and at every tenth (or hundredth) incoming pulse, a relay is operated by the scaler which actuates a striker. This striker is mounted directly above the tip of the collimator and lies on the axis of the cylindrical hole. A piece of carbon paper, with white paper underneath, is affixed to a flat glass plate held in a horizontal plane above the patient so that the striker, on being actuated, strikes the carbon paper and leaves a record in the form of a black dot on the white paper. Accordingly, in any traversal, the frequency with which the dots appear in any segment gives a measure of the amount of radioiodine in the field of view of the detector at that position.

It will be noticed from the illustrations which follow that dots appear over portions of tissue which contain no radioiodine; these are due to "background". Background is undesirable, since it tends to mask regional changes within the gland, and considerable effort is being expended to reduce it to low limits. The newer instruments are quite successful in this regard but at a considerable increase in cost. There are as well devices for automatically subtracting background, leading to dramatic scans in which the thyroid is outlined with little or no surrounding background. This is, however, simply a convenience, and unlike reduction of background does not lead to scans which are inherently more accurate.

Lack of depth discrimination in scanning remains the most serious limitation of the technique. Francis, Bell

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*It is implied here that the transverse movement is along a straight line perpendicular to the longitudinal axis of the body. For most scanners this is true. However, with the scanner used in the present work, the detector described arcs of circles, the radii of which were varied in obtaining the map. This method of construction is not desirable. It was originally chosen solely for reasons of economy, and has since been discarded.

and Harris[3] have designed a collimator with focusing properties, which goes part way to solving the problem, but the depth of focus is not sufficiently short to allow one to pick out narrow layers of tissue, or to examine small nodules without interference from radioiodine in paranodular tissue. Nevertheless, the focusing collimator is a definite improvement, and hope can be held out for further development along these lines.

RESULTS

Nodular Goitre

In this discussion a nodule is defined as a discretely palpable mass of thyroid tissue, 1 cm. or greater in diameter, to be distinguished from localized or diffuse lobulation. Nodular goitres are extremely common and a major clinical problem which they pose is the detection of the relatively uncommon cases with carcinomatous nodules. It has been frequently emphasized that the incidence of carcinoma in the solitary thyroid nodule is considerably greater than in multinodular goitre,[4, 5] and on this basis it has been recommended that all persons with solitary nodules be submitted to surgery. However, many goitres which on clinical examination appear to contain a single nodule prove to be multinodular at time of pathological examination, and if surgery is performed on all such cases, a large number of unnecessary operations will be carried out. It is in this situation that mapping of thyroid nodules may be of value. On the basis of the avidity for I^{131}, nodules have been classified into three groups. When the uptake of I^{131} is greater than that of the paranodular tissue, the nodule is referred to as a "hot" nodule; when less, "cold"; and when equal to it, "warm".[7]

Thyroid carcinoma has rarely been detected in "hot" or "warm" nodules. The experience of previous investigators indicates that most thyroid carcinomata pick up little or no radioiodine and fall into the category of cold nodules.[7] This appears to be true whether the nodules show diffuse or spotty areas of diminished function.[6, 7]

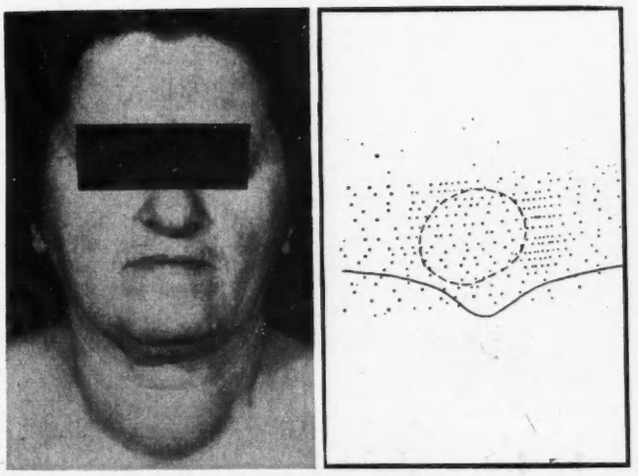

Fig. 1.—Photograph of patient with goitre and *in vivo* distribution of I^{131} showing a cold nodule, which resulted from a thyroid carcinoma.

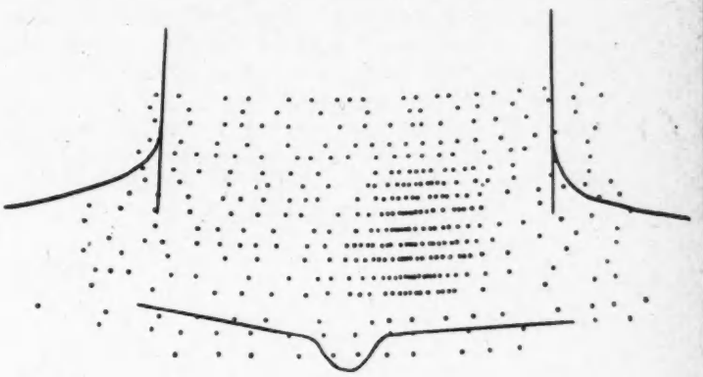

Fig. 2.—Neck scan showing absence of I^{131} uptake on the right, resulting from a large calcified adenoma.

CASE 1.—A 50-year-old patient was aware of goitre for ten years with increase in size for the past five years. There were no clinical or laboratory findings of hypothyroidism or hyperthyroidism. Fig. 1 shows the appearance of the goitre and the preoperative neck scan. It will be observed that most of the I^{131} appears on the left and at the periphery of the nodule on the right; the radioactivity in the remainder of the gland is not appreciably greater than that present in the extrathyroidal neck tissue. Pathological examination showed that the non-functional area of thyroid was associated with a large nodule having the histological appearance of solid thyroid carcinoma.

CASE 2.—A 60-year-old man had noticed the presence of goitre for many years. Examination revealed a large hard nodule present in the right lobe of the thyroid. The neck scan (Fig. 2) showed no radioactivity in the nodular area. At operation, a calcified adenoma was found.

Thus it must not be inferred that all cold nodules are carcinomatous, for lack of activity may be observed in calcified adenomata, cysts, and organized hæmatoma, as illustrated by Case 2. The finding that a nodule is cold, however, is one point which favours the diagnosis of thyroid carcinoma and surgical intervention. Observations on large series of patients have suggested that some 20% of non-functioning single thyroid nodules are carcinomatous.[7]

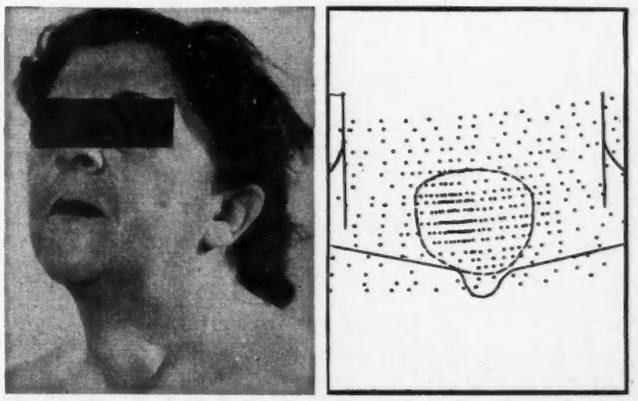

Fig. 3.—Photograph and scan of neck showing outline of goitre. The right side is the site of a nodule which appears to be hyperfunctional.

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CASE 3.—A 46-year-old woman had noted the presence of a large midline goitre for four years; four months before her first clinic visit symptoms of hyperthyroidism developed. Fig. 3 shows a photograph of this patient and the conventional scan which suggests that the nodule is partially hyperfunctional. A scan taken in the lateral position, however (Fig. 4), revealed that the nodule was in fact cold.

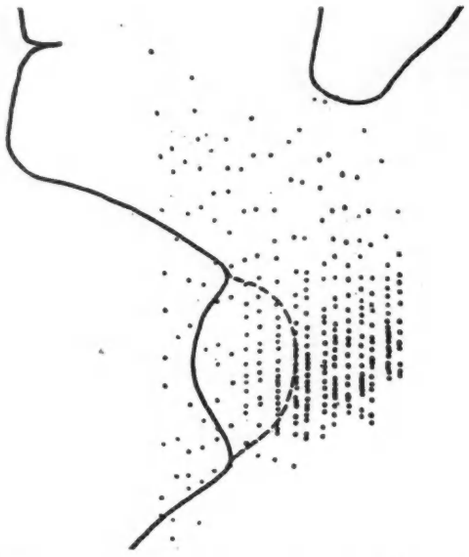

Fig. 4.—Scan of neck on same patient as that shown in Fig. 3, in lateral position, showing that the thyroid nodule previously thought to be hyperfunctional is in fact hypofunctional. The radioactivity in the underlying tissue masked the coldness of this nodule.

This case serves to illustrate that the lack of function in a nodule may be obscured by radiation present around or behind the nodular area; as noted previously, this constitutes a distinct inadequacy of the technique. The lateral view is practicable only in selected patients, particularly those with large goitres.

Differential Diagnosis of Extrathyroidal Masses

CASE 4.—Fig. 5 shows the chest radiograph of a patient in whom there was doubt about the nature of a superior mediastinal mass. The scan clearly indicates that it was associated with the cervical thyroid, took up I^{131} and was therefore mediastinal thyroid.

The technique of scanning has in our experience been useful in the differential diagnosis of mediastinal masses. Uptake of radioiodine by such a mass proves that one is dealing with a mass of thyroid origin. Failure of uptake, however, does not rule out the presence of thyroid tissue with little avidity for I^{131}.

CASE 5.—A 48-year-old woman with bone pain was found in the course of radiological investigation to have multiple metastatic lesions in her skeletal system. The primary site was undetermined and because of her severe debility exploration of a retrosternal goitre (a possible source of origin) was not carried out. Fig. 6 shows a radiograph of the left side of the pelvis, and the accompanying scan. The lesion exhibited uptake of radioiodine, indicating the presence of metastatic thyroid carcinoma.

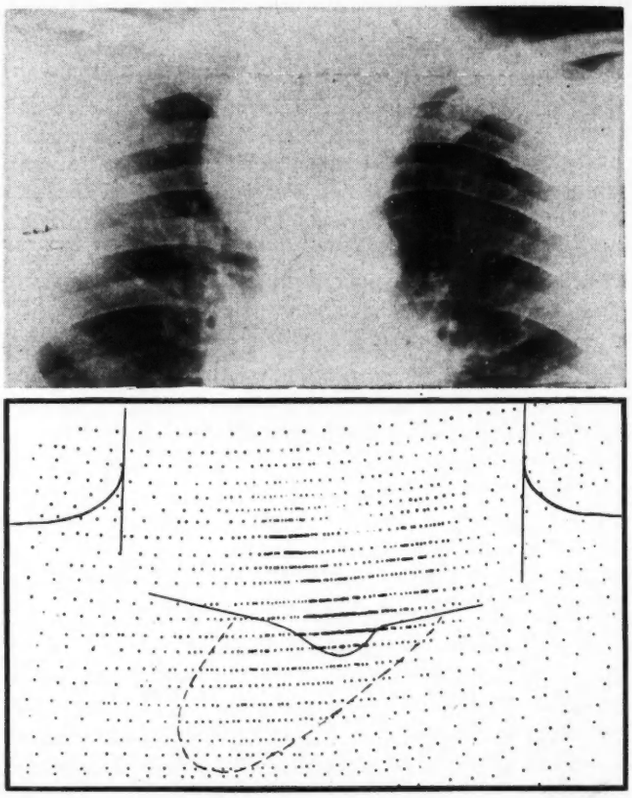

Fig. 5.—Chest radiograph showing presence of superior mediastinal mass, and scan showing that this mass was associated with cervical thyroid, was avid for I^{131} and, therefore, was a mediastinal goitre.

The technique, therefore, is of value in demonstrating that a known metastatic lesion is of thyroid origin. There are cases in which scanning may demonstrate the presence of metastatic lesions not apparent on radiological examination, but the method is of value only in those thyroid metastases which show avidity for iodine. Since functional thyroid carcinoma metastases are sometimes amenable to radioiodine therapy, scanning is important in determining the feasibility of this form of treatment.

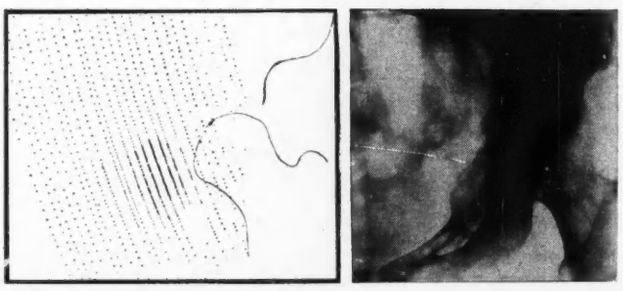

Fig. 6.—Radiograph of pelvis on right shows metastatic lesion in ilium and pubic ramus. This lesion was detected independently by scintography as shown by the area of increased I^{131} uptake in the scan on the left.

Hyperthyroidism

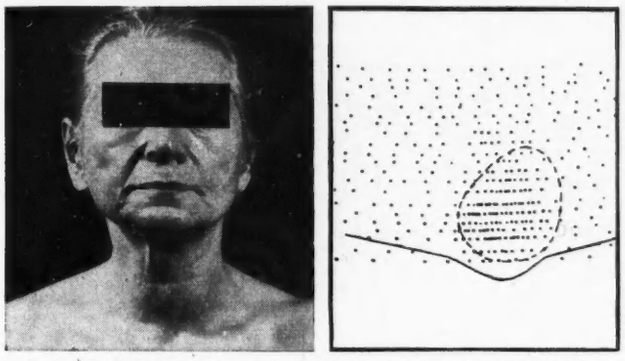

Fig. 7.—Photograph and neck scan of patient with multinodular goitre and hyperthyroidism. The scan shows all the radioactivity to be concentrated in the left lobe. See text.

CASE 6.—This patient suffered from hyperthyroidism of five years' duration associated with multinodular goitre. The scan (Fig. 7) showed all the radioactivity to be concentrated in one large nodule in the left lobe. The surgeon performed a left lobectomy, which resulted in complete remission of the hyperthyroid state.

Scanning does not play a major role in the clinical assessment of a hyperthyroid patient; its main use here is as a tool for clinical research into the mechanisms of hyperthyroidism. Nevertheless, as shown by Case 6, it may at times be of value to the surgeon in performing subtotal thyroidectomy. While long-term follow-up is necessary in such patients before any general conclusions can be drawn, it is possible that the technique may be used as a guide to the extent of surgery and thus aid in reducing the incidence of complications after operation.

SUMMARY

We have attempted in this brief review to assess the status of neck scanning as an investigative tool in thyroid disorders. Technical aspects are now well developed and further advances may be expected. At present, scanning is of aid in the evaluation of a nontoxic nodular goitre, particularly in selection of patients with single nodules for thyroidectomy. In establishing the nature of extrathyroidal masses, mediastinal or metastatic, it is of concrete value. It may prove to be of value in guiding the surgeon in the performance of subtotal thyroidectomy, so that the incidence of complications after operation is reduced. While more experience is required before its final role is established, it is a laboratory tool of considerable promise.

We would like to thank Mr. N. Feifer for preparation of the photographs.

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RÉSUMÉ

Une des épreuves employées dans l'exploration fonctionnelle de la glande thyroïde par l'iode radioactif est celle qui consiste à établir la cartographie différentielle de l'organe grâce à un compteur à scintillations à collimateur, relié à un dispositif d'enregistrement automatique sur papier. Ce procédé que les Anglo-Saxons appellent *"scintiscanning"* offre des avantages appréciables dans la localisation et l'identification de certaines lésions thyroïdiennes comme le goitre nodulaire ou les nodules isolés. On peut aussi s'en servir pour différencier les masses extrathyroïdiennes médiastinales ou métastatiques, ou pour guider le chirurgien dans les thyroïdectomies subtotales. Cette méthode se prête à une bonne définition de l'exploration et semble pleine d'avenir.

THE CHRONIC SUBCUTANEOUS TOXICITY OF SPIRAMYCIN ADIPATE*

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SPIRAMYCIN (Rovamycine—Poulenc) is an antibiotic agent extracted from *Streptomyces amb*o*faciens*,[6] a fungus found in the soil of northern France.[7] It has an antibacterial spectrum similar to that of erythromycin[10] and oleandomycin.[9] Spiramycin is available in powder form and as tablets, each containing 250 mg. of the base. It may be classified with erythromycin, vancomycin, oleandomycin and novobiocin, as an antibiotic substitute for penicillin. Spiramycin is indicated in the treatment of infections against which it may be effective, provided resistance or cross-resistance has not developed.

Before using a new drug it is useful to have information upon what may happen if an excessively large or toxic dose is given or taken at one time (acute poisoning) or over a long period of time (chronic poisoning). Oral doses of the order of 5 g. per kg. body weight in dogs and 10 g. per kg. in albino rats have been found to produce a fulminating gastroenteritis, necrosis of the liver and kidneys, and death in half the animals.[2] It has been estimated that similar effects would be produced in man by an oral dose of 1 to 2 g. per kg. if the drug is not vomited.[2] Chronic oral ad-

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ministration of spiramycin in a dose of one-tenth the above LD50's per day for two months produces a systemic toxæmia and some deaths in dogs and albino rats.[4, 5] Subcutaneous administration of 3.5 g. per kg. in the albino rat produces a violent inflammation at the site of injection, renal tubular necrosis, lesser toxic effects upon a variety of other body organs, and death in half the animals.[3]

Toxic effects from chronic daily subcutaneous injection of spiramycin have not been previously described. It is with this aspect of the toxicology of spiramycin that the present report is concerned.

METHOD

The study was made upon young, male, albino rats originally of a Wistar strain which has been inbred in the animal quarters of the Department of Pharmacology at Queen's University for the past 20 years. The animals were selected immediately after weaning and divided into three dosage groups in such a way that each rat had at least one littermate in each of the other groups. This experimental design permitted a twin-analysis (of non-independent variables[8]) of resulting data. Because the rats fought with each other after injection of spiramycin adipate, they were housed singly in individual cages. They were fed Purina fox chow checkers and water *ad libitum*.

Spiramycin was administrated as a sterile 4.00% (w/v) solution of the adipate in distilled water. The solution was prepared just before each daily subcutaneous injection into the dorsal thoracic region. Two doses of the antibiotic agent were selected for chronic daily injection, one equal to approximately 0.05 and the other to 0.15 the acute LD50 in albino rats by subcutaneous injection. The doses were 0.17 and 0.52 g. per kg. body weight of spiromycin base, or 0.2 and 0.6 g. of spiramycin adipate respectively. The first dose was given daily, seven days a week, to ten rats. The larger dose was administered at the same intervals to nine rats. A third group of nine control rats, twins of the above, received a daily injection of sterilized isotonic saline.

Body weight was measured daily. Food intake and water intake were measured weekly. Every fortnight locomotor activity was determined and samples of blood and urine were obtained for a series of measurements. Food intake was measured as g. chow per kg. body weight per 24 hours, and water intake as ml. water per kg. per 24 hours. On each sample of blood, an erythrocyte count, leukocyte count, and hæmoglobin estimation were made. On a sample of urine collected in a metabolism cage were determined volume (calculated as ml. per kg. body weight per 24 hours), specific gravity, pH, albumin, sugar, acetone, blood, bile pigments, and indican. Locomotor activity was measured in Wahmann activity units over 24 hours and expressed as revolutions of the drum, as read off the Veeder counter, per rat per 24 hours.

The above measurements were continued until death of albino rats receiving the larger dose, and for 8 to 10 weeks, when definite evidence of toxæmic influence was present, on rats receiving the smaller dose. Animals in the latter group were anæsthetized with chloroform-ether, a sample of 10 to 15 ml. of heparinized blood was obtained by cardiac puncture, and rats were killed with chloroform. A hæmatocrit was determined upon the heparinized blood, and a sample of blood plasma extracted with alcohol-ether and analyzed for total lipid, neutral fat, total fatty acids, total cholesterol, ester cholesterol, free cholesterol, and phospholipid by the method of Boyd.[1] At the same time as these latter measurements were made upon a spiramycin-treated rat, its control twin was treated in the same way.

All rats were autopsied after death. Studies made at autopsy included observation of the gross lesions, microscopic examination of sections stained with hæmatoxylin-phloxine-saffron, water concentration, and wet and dry weight of the organs noted in Tables I and II.

TABLE I.—THE WATER LEVEL OF ORGANS REMOVED AT AUTOPSY FROM ALBINO RATS AFTER SUBCUTANEOUS ADMINISTRATION OF SPIRAMYCIN ADIPATE IN A DOSE OF 0.2 G. PER KG. BODY WEIGHT PER DAY FOR 8 TO 10 WEEKS

Organ	*Water level as g. water per 100 g. dry weight in controls (Mean ± S.D.)*	*Mean difference in spiramycin—treated rats (% of mean in controls)*	*Probability (P) that mean difference equals zero*
Skin, site of injection	208 ± 16	+52.3	<0.001
Mesentery-omentum	111 ± 34	+51.4	0.005
Abdominal muscle	284 ± 16	+27.1	<0.001
Small bowel	448 ± 33	+14.3	<0.001
Colon	460 ± 46	+12.8	0.005
Kidneys	310 ± 12	+12.6	<0.001
Residual carcass	226 ± 11	+ 9.3	0.02
Liver	237 ± 5	+ 7.6	<0.001
Skin	208 ± 16	+ 6.7	0.05
Stomach	349 ± 19	+ 6.6	0.001
Thymus gland	339 ± 20	+ 5.3	0.1
Spleen	339 ± 33	+ 5.3	0.2
Heart	358 ± 8	+ 2.8	0.02
Lungs	371 ± 10	+ 2.2	0.1
Cæcum	439 ± 27	+ 0.9	0.8
Brain	363 ± 19	+ 0.8	0.7
Testes	648 ± 35	- 2.0	0.3
Adrenal glands	303 ± 70	- 9.9	0.2

RESULTS

A. *Effects of 0.2 g. per kg. per day.*

The injection produced pain and irritation. Hyperreflexia and strychnine-like convulsions appeared within the next hour. Some necrosis developed in the skin at the sites of injection and the lesions healed with slight scar formation. Otherwise, the animals appeared normal to casual observation.

Systemic toxic effects of this dose could be proven as early as after seven days of administration. At this time body weight and food intake were significantly ($P = 0.025$) below those of the control twins. Locomotor activity was found de-

TABLE II.—THE DRY WEIGHT OF ORGANS REMOVED AT AUTOPSY FROM ALBINO RATS AFTER SUBCUTANEOUS ADMINISTRATION OF SPIRAMYCIN ADIPATE IN A DOSE OF 0.2 G. PER KG. BODY WEIGHT PER DAY FOR 8 TO 10 WEEKS

Organ	*Dry weight (g.) of control rats (Mean ± S.D.)*	*Mean difference in spiramycin-treated rats (% of mean in controls)*	*Probability (P) that mean difference equals zero*
Abdominal muscle	3.55 ± 0.89	-40.0	<0.001
Skin	18.4 ± 3.2	-34.8	<0.001
Thymus gland	0.0671 ± 0.0150	-29.1	0.001
Residual carcass	48.2 ± 5.8	-27.9	<0.001
Mesentery-omentum	1.50 ± 0.60	-21.3	0.1
Testes	0.396 ± 0.034	-12.9	0.001
Kidneys	0.518 ± 0.083	-12.9	0.05
Small bowel	1.67 ± 0.25	-12.0	0.05
Lungs	0.275 ± 0.042	-12.0	0.1
Colon	0.376 ± 0.049	-10.6	0.1
Cæcum	0.206 ± 0.024	- 8.3	0.2
Brain	0.407 ± 0.039	- 7.4	0.05
Spleen	0.191 ± 0.034	- 6.8	0.5
Heart	0.203 ± 0.025	- 5.9	0.3
Stomach	0.326 ± 0.048	- 4.3	0.5
Liver	3.70 ± 0.48	+ 3.8	0.7
Adrenal glands	0.00839 ± 0.00180	+95.4	<0.001

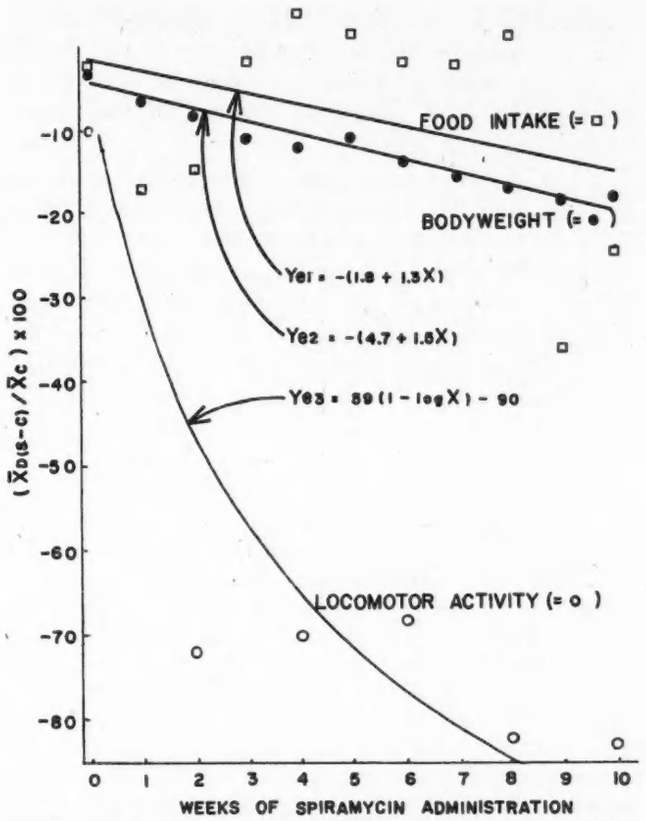

Fig. 1.—Mean differences in the food intake (Ye1), body weight (Ye2), and locomotor activity (Ye3) of albino rats receiving spiramycin adipate (Xs), in a dose of 0.2 g. per kg. per day subcutaneously, and their twin controls (Xc).

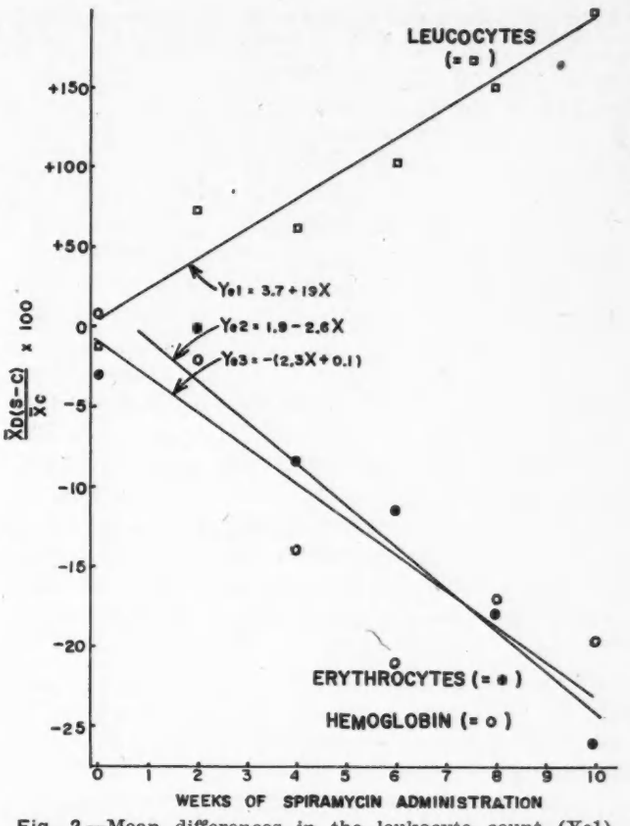

Fig. 2.—Mean differences in the leukocyte count (Ye1), erythrocyte count (Ye2), and hæmoglobin concentration (Ye3) of albino rats receiving spiramycin adipate (Xs), in a dose of 0.2 g. per kg. per day subcutaneously, and their control twins (Xc).

pressed at the end of two weeks. As illustrated in Fig. 1, these differences persisted throughout the period of treatment to a greater or lesser degree.

The concentration of blood hæmoglobin became significantly ($P = 0.02$) less than that of the controls after four weeks. The red blood cell count was significantly ($P = 0.01$) less after six weeks. Accompanying the anæmia there was a leukocytosis. The results have been illustrated graphically in Fig. 2.

The spiramycin-treated rats drank significantly ($P = 0.01$) more water from the 4th to the 8th week. There were three statistically significant shifts in the volume of urine. Urinary volume was increased at four weeks, returned to control values at six weeks, and rose again at eight weeks. These changes have been plotted in Fig. 3.

The specific gravity of urine was less than that of the controls except at six weeks. Indican was not present in urine. The urinary acidity was not affected. Positive tests for albumin and blood were recorded occasionally in both spiramycin-treated and control rats. Tests for glucose, acetone, and bile pigments were negative in urine from both groups.

At autopsy, pallor was noted in many organs such as the pyloric stomach, small bowel, colon, mesentery, liver, kidneys, spleen, adrenal glands, and skeletal muscle. The adrenals were visibly enlarged. Inflammation at the site of injection was seen to have spread to adjacent muscles and to the peritoneum. Adhesions were encountered on the posterior surface of the liver and kidneys. The entire skin was removed and the residual carcass homogenized in a Waring blendor. The resulting homogenate was more watery than that of the controls.

Values for the water content of organs removed at autopsy have been summarized statistically in

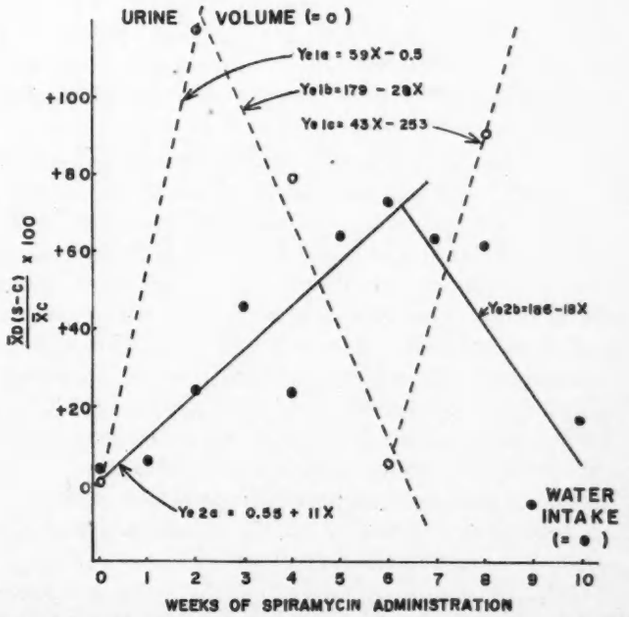

Fig. 3.—Mean differences in the volume of urine (Ye1a, Ye1b, and Ye1c), and intake of water (Ye2a and Ye2b) of albino rats receiving spiramycin adipate (Xs), in a dose of 0.2 g. per kg. per day subcutaneously, and their control twins (Xc).

TABLE III.—LEVELS OF PLASMA LIPIDS AND THE HÆMATOCRIT IN ALBINO RATS AFTER 8 TO 10 WEEKS OF ADMINISTRATION OF SPIRAMYCIN ADIPATE IN A DOSE OF 0.2 G. PER KG. BODY WEIGHT PER DAY SUBCUTANEOUSLY

Measurement	*Levels in control twins expressed as mg. per 100 ml. (mean ± S.D.)*	*Mean difference in spiramycin-treated twins (% of control mean)*	*Probability (P) that mean difference equals zero*
Total lipid	233.0 ± 21.0	+30.9	<0.001
Neutral fat	105.0 ± 20.0	+20.0	0.02
Total fatty acids	157.0 ± 10.0	+27.4	<0.001
Total cholesterol	55.0 ± 12.0	+34.5	0.001
Ester cholesterol	38.0 ± 10.0	+23.7	0.02
Free cholesterol	17.0 ± 4.0	+58.8	0.01
Phospholipid	48.0 ± 26.0	+54.2	0.02
Hæmatocrit	53.0 ± 2.0	−16.4	<0.001

Table I. There was a more or less generalized œdema.

Values for dry weights of these organs have been summarized in Table II. Loss of dry weight was marked in skeletal (lateroventral abdominal) muscle, skin, thymus gland, and residual carcass. It was less extensive in testes, kidneys, small bowel, and brain. Dry weight of the adrenal glands was increased.

The results summarized in Table III indicate that there was a lipæmia. The hæmatocrit of the pre-mortem blood samples was less than that of the controls.

Microscopically, pathological changes were seen in the liver, kidneys, adrenal glands, skeletal muscle, and in sections of skin taken at the site of injection. The histopathologic damage was similar qualitatively to that seen in animals receiving the larger daily dose and will be described below.

B. *Effects of 0.6 g. per kg. per day.*

The toxic changes in these animals were similar to those in animals receiving the smaller dose, but they progressed further and more rapidly. There was considerable necrosis and sloughing of the skin at the site of injection. Two animals had chromodacryorrhœa during the second week. Two rats died on the 12th day, two on the 15th, two on the 17th, and one on each of the 22nd, 30th, and 38th days.

At autopsy, there was microscopic evidence of a more or less generalized toxæmia. In the kidney, there was œdema of Bowman's capsule, the glomerulus, and the loop of Henle, and necrosis of the convoluted tubules, especially the distal tubules. The hepatic cords were pale and granular and the Kupffer cells were swollen. The pyloric zymogenic cells of the stomach were shrunken. The goblet cells of the intestinal crypts of Lieberkühn were dilated. There were degenerative changes in the lining epithelium and lamina propria of the gastro-intestinal tract. There was a deficiency of zymogenic granules in the pancreas, and the islets of Langerhans were anæmic.

Cells of the three zones of the adrenal cortex were swollen and vacuolated and the adrenal sinusoids contained but few erythrocytes. There was no sperm in the testes and the spermatocytes were multinucleated. In the spleen, the number of lymphocytes was decreased in the white pulp, the cords of Billroth of the red pulp were swollen and pale, and the splenic sinusoids contained few red cells.

Cardiac muscle was pale and granular, and the A discs and intercalated discs were less evident than in the controls. Cross striation was deficient in skeletal muscle. Capillary vasodilatation was found occasionally in the lungs and meninges. Various stages of inflammation appeared in sections of the skin taken at sites of injection of spiramycin adipate.

SUMMARY

Spiramycin adipate injected subcutaneously every day in a dose of 0.6 g. per kg. body weight killed young albino rats in 2-5 weeks. Similar injections of 0.2 g. per kg. killed no rats over a period of 8-10 weeks but did produce signs of toxæmia. The injection was irritating and caused an inflammation of the skin and adjacent tissues. Growth rate was depressed. Food intake was sporadically reduced. The animals drank more water and diuresis was commonly seen. Locomotor activity was less than that of the controls. An anæmia and a leukocytosis developed. A lipæmia was found just before sacrifice of animals receiving the lower dose. At autopsy a necrosis of the renal tubules was found. Most organs of the body were œdematous and several had lost dry weight. Evidence of further toxic damage was found microscopically in various organs such as the liver, pancreas, heart, testes, adrenal glands, thymus gland, spleen, and skin. The cause of death was subacute nephritis associated with a generalized toxæmia due to chronic administration of toxic doses of spiramycin adipate.

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RÉSUMÉ

La base de spiramycine (adipate) injectée par voie sous-cutanée à dose quotidienne de 0.6 g/kg. entraîna la mort de jeunes rats albinos en deux à cinq semaines. Ces rats survécurent à des injections semblables mais à dose de 0.2 g/kg. pendant huit à dix semaines; ils montrèrent cependant des signes de toxémie. La peau et les tissus avoisinants devinrent enflammés par l'irritation des injections; le taux de croissance diminua; l'appétit fluctua, et de l'anémie, de la leucocytose et de la lipémie apparurent. Ces animaux burent plus d'eau que d'habitude; on observa des diurèses à plusieurs reprises, et leur activité locomotrice fut moindre que celle des rats témoins. A l'autopsie on découvrit de la nécrose des tubes contournés; la plupart des viscères étaient œdématiés bien qu'ils aient perdu de leur substance. L'examen histologique révéla d'autres altérations toxiques dans plusieurs tissus. La mort fut causée par une néphrite sub-aiguë, accompagnée d'une toxémie généralisée causée par l'administration répétée de doses toxiques de spiramycine.

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INFANTILE SCURVY IN MANITOBA

[Some notes on the history of scurvy in the Province and a review of 33 cases seen at the Children's Hospital of Winnipeg, 1953-56.]

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HISTORICAL NOTES

ANYONE INTERESTED in scurvy is soon aware that Canada has had more than a passing acquaintance with this disease. The first reported postmortem examination in Canadian history was on Philippe Rougemont, one of Jacques Cartier's adventurers, who died of fulminant scurvy. Cartier in 1535, spending his first winter on the St. Charles River near the present city of Quebec and with most of his 110 Frenchmen ill with scurvy, had a barber surgeon perform this autopsy, hopeful that he might find a remedy for the *"grosse maladie"*.

"The disease wholly unknown to us as it was broke out among us with amazing severity. Some lost their very substance and their legs became swollen and puffed up while the sinews contracted and turned coal-black and in some cases all blotched with drops of purplish blood. Then the disease would creep up to the hips, the thighs and shoulders, arms and neck. And all the sick had their mouths so tainted and their gums so decayed that all the flesh peeled off down to the roots of their teeth which the latter almost all fell out in time."[1] The examination over, "we buried the body as best we could. May God in His holy grace have mercy on his soul and those of all the dead." A clue to the remedy was not forthcoming and all would surely have perished but for an Indian, Dam Agaya, Cartier's one-time interpreter, who himself recently sick with the disease but miraculously improved revealed the remedy known to his people of bark and leaves of the white spruce tree made into a decoction.

The first account of scurvy in what is now Manitoba concerned Jens Munk who under the patronage of the King of Denmark sailed his two ships, "Unicorn" and "Lamphrey" to Canada in 1619 and was compelled to spend the winter on the Churchill River. Scurvy and extreme cold took their toll of his crew until only himself and two of his men were left alive. They just succeeded in setting sail for Norway after "they had sucked the roots of every green sprout within reach."[2]

In the "Letters Outward" of the Hudson's Bay Company, dated June 1693, is the following reference to scurvy: "Wee desire a bottle or two of that Juyce that you tap out of the trees wch you mixt with your drink when any one is troubled with the scurvy or if you have plenty of it that you would send more with Directions how to use it there."[3]

In May of 1814, William Auld, surgeon to the Hudson's Bay Company, makes reference to the Selkirk settlers having suffered scurvy during the two preceding winters. "A disease entirely occasioned by salted and weak food."[4]

Scurvy is again reported in Manitoba in 1875, when in consequence of a grasshopper plague causing a great scarcity of fresh vegetables several of the patients at the Selkirk Mental Hospital were stricken with the disease.[5]

In the early accounts of scurvy in Manitoba as elsewhere little mention is made of children, probably because breast feeding was common practice and the disease is all but unknown amongst the breast-fed. In earlier times the hand-fed infant often died in the early months of life, and even in the event of survival and the development of scurvy it was likely confused with rickets until 1883, when Barlow published his classical paper clearly identifying scurvy.[6] The disease was increasingly recognized as artificial feeding became more common; and as the heat sterilization of cow's milk became more efficient the incidence of scurvy further increased. This was understandable, since cow's milk is by the nature of things a weak antiscorbutic, the calf for which it was intended being capable of synthesizing its own vitamin C. In this present era of infant parasitism on the cow, it is not surprising to find that the last words in the history of scurvy remain to be written.

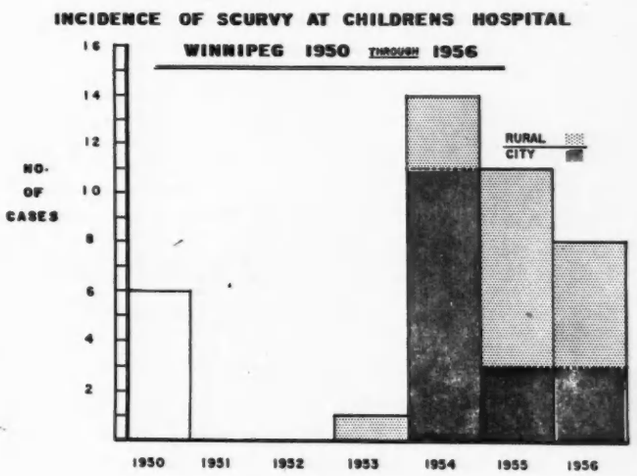

Fig. 1.

In December of 1953, a nine-month-old infant presented at the Children's Hospital, Winnipeg, with a history of pain in the legs of three weeks' duration. His mother stated, "He seems sore every place he is touched." A provisional diagnosis of poliomyelitis had been made by the referring doctor, this disease being endemic in Manitoba at that time. A closer scrutiny revealed, however, a petechial rash, bleeding gums, acute angulation at the costo-chondral junction and a paralysis more apparent than real. He had in fact advanced scurvy, and the ensuing months have seen a regular influx of infantile scurvy unusual in any recent period at the Children's Hospital. The incidence is shown in Fig. 1.

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INCIDENCE OF SCURVY AT CHILDREN'S HOSPITAL, WINNIPEG

A study of the 33 cases of infantile scurvy presenting during the period 1953 through 1956 forms the basis of this report. There were no deaths.

Age and Sex Incidence

There were no cases before 6 months of age. The majority occurred between the age of 6 and 12 months. There was, however, an isolated case at 16 months and two others at 36 months of age. The two children aged 36 months were interesting; one presenting a behaviour problem had persistently refused solid foods and in fact all kinds of food other than milk, and the other was a hydrocephalic, mentally defective child and very difficult to feed. The age incidence is shown graphically in Fig. 2.

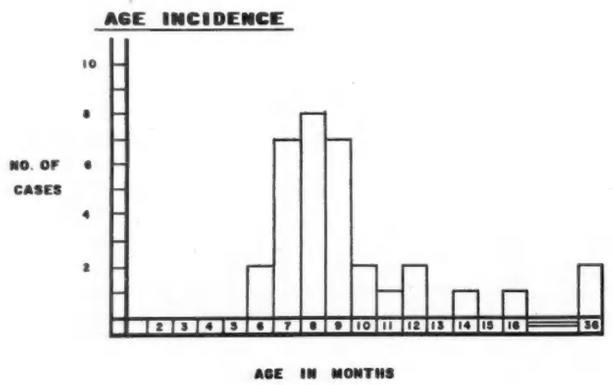

Fig. 2.

The sex incidence was essentially equal with 15 male and 18 female infants affected.

Domicile

The city of Winnipeg and rural Manitoba were equally represented with 16 cases each (Table I). The estimated population of Winnipeg in 1956 was 409,687 and the estimated population of rural Manitoba in 1956 was 440,353. Table I shows the location of cases and gives some indication of their widespread distribution in rural Manitoba. There was one case from Western Ontario.

TABLE I.—DOMICILE OF PATIENTS

Winnipeg		16
Rural Manitoba		16
	Anama Bay	St. Germaine
	Dickens	Shoal Lake
	Eriksdale	Siglunes
	Holland	Souris
	Loon Straits	Steinbach
	Matheson Island	Wheatlands
	Rivers	Winnipegosis
	St. Ambrose	Winnipegaw
Other (Sioux Lookout, Ontario)		1

Reason for Hospital Referral

It is notable that of the 33 infants with scurvy, 18 were referred to hospital by a physician but only 4 were correctly diagnosed (Table II). It should be appreciated that scurvy was seldom an incidental finding in this reported series. The illness precipitating hospital admission was referable directly to the scorbutic process. A lack of clinical awareness of scurvy is inferred.

TABLE II.—REASON FOR HOSPITAL REFERRAL

Referred by	*No.*	*Reason given*	*No.*
Physician	18	Scurvy—diagnosis correct	4
		Paralysis not otherwise specified	2
		Paralysis and meningitis	1
		Poliomyelitis	1
		Septic arthritis	1
		Anæmia and intractable fever	1
		Kidney infection (this infant had hæmaturia)	1
		Pyrexia of unknown origin	1
		"For investigation"	4
		Undescended testicles and possible rickets	1
		"Colic"	1
Public health nurse or V.O.N.	2	Meningitis	1
		Dehydration	1
Indian health agent	1	Painful limbs	1
Outpatient service, other hospital	1	Irritability and vomiting	1
Parents on own account (public hospital service)	11	"Irritability", "Pain in legs", "Tenderness in legs", "Won't stand up", etc.	11
	33		33

In 11 cases the child was brought to the Public Outpatient Service by the parents. The following are some of the verbatim remarks: "He seems to have pain in the legs. He used to stand but won't even try now." "She seems to have pain in the legs and knees and screams when her legs are touched." "She used to sit happily but now when sat up she whimpers all the time." "His legs have become very tender and he screams and cries if his legs are touched even with the bed clothes." "His arms are floppy and he hasn't been moving the left leg as much as before."

Symptomatology

The prevailing symptoms are shown in Fig. 3.

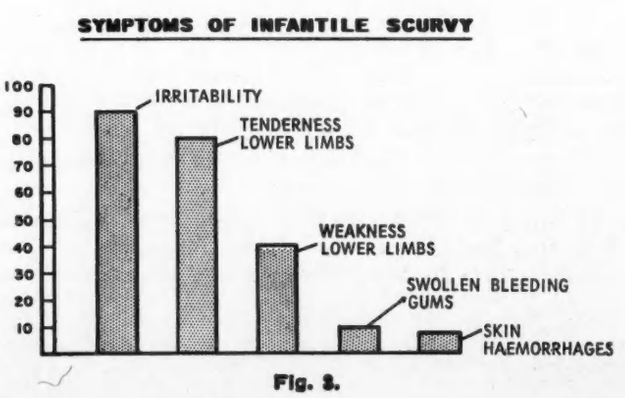

Fig. 3.

Irritability was often marked and especially manifest with handling of the infant or his anticipation of this. Tenderness of the lower limbs was often noted at the time of diaper changing. Weakness and sometimes loss of movement, usually of the lower limbs, was often shown by regression of sitting, standing or walking skills and interest.

Place in Family

Thirty-two of the 33 children had brothers or sisters, but in no instance was there any family history of scurvy elicited either from interviewing the parents or from hospital records. The largest family was one of 10 children and from this came one of the most florid examples of scurvy with massive periorbital hæmorrhage. The average number of children to a family was four.

Economic Status

An indication of the socio-economic environment of the reported cases is given from the father's occupation listed in Table III.

TABLE III.—ECONOMIC STATUS

Unemployed, family on public welfare	8 cases
Labourer	7 "
Indian or Metis, employment vague	6 "
Armed forces (non-commissioned rank)	5 "
Skilled or semi-skilled work	4 "
No record	3 "

In two-thirds of the cases the children were from amongst the less privileged ranks of society.

Previous History (Table IV)

All but three were mature infants of normal weight at birth. There were three premature infants, a finding which suggests no particular bias to the development of scurvy in the premature. In only 6 of the 33 cases was there evident previous ill-health.

TABLE IV.—PREVIOUS HISTORY

Pyloric stenosis	1 case
Recurrent upper respiratory infection	1 "
Severe behaviour problem	1 "
Mental retardation	3 cases
Hydrocephalus following difficult premature birth.	
Hydrocephalus following massive brain abscess.	
Cerebral agenesis.	

PHYSICAL FINDINGS

The prevalent physical signs are indicated in Fig. 4.

Irritability—94% of cases.

This was apparent as soon as the child was examined. Left alone, he lay quietly in his crib but with the approach of anyone towards him he might anticipate the handling of his tender limbs and cry out.

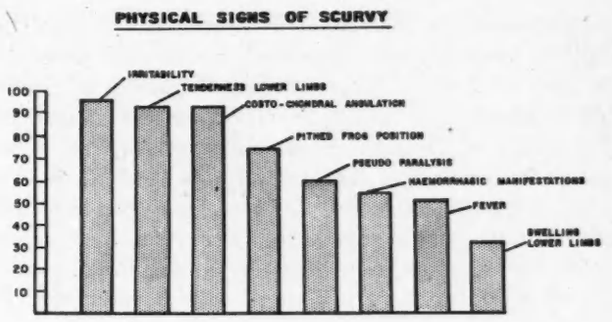

Fig. 4.

Tenderness of the lower limbs—91% of cases.

Tenderness affected both legs, although often one more than the other. The cause of this tenderness remains obscure. It existed whether or not there was x-ray evidence of subperiosteal hæmorrhage. Furthermore, antiscorbutic treatment relieved the tenderness promptly, long before any signs of resolution where subperiosteal hæmorrhage was present.

Costo-chondral swelling or angulation—91% of cases.

Whilst this was sometimes apparent on inspection as a beading effect, it was best appreciated by palpation when, because of subluxation of the cartilaginous anterior chest wall on the bony lateral portion, a sense of acute angulation at the costo-chondral junction was experienced. This effect has been referred to as a "bayonet deformity", because of its resemblance to the drop between the barrel of a rifle and its fixed bayonet. The acute angulation effect, because of its regular appearance and easy appreciation, was a most useful diagnostic sign. The acute angulation effect of scurvy has been stated to be distinctive from the beading effect resulting from expansion of the costo-chondral junction characteristic of rickets. It is not always easy to make this distinction, however.

The *"pithed frog"* position was a feature in 76% of cases.

It appeared to be a position of comfort and was so striking that it should at once raise suspicion of scurvy in an infant of appropriate age.

Pseudo-paralysis—60% of cases.

This was usually apparent in the lower limbs. It is presumably related to the above-noted position of comfort, movement from which induces pain.

Fever.

Fever implying a rectal temperature in excess of 101° F. at the time of admission was present in 54% of cases. The fever did not appear dependent upon intercurrent infection, since only two of the 33 cases showed any significant signs of infection (an upper respiratory infection in both instances). In 4 of 17 cases, antibiotic as well

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as antiscorbutic therapy was administered but the fall in temperature appeared to be independent of the antibiotic, the average duration of fever after admission being seven days. In one case penicillin, chloramphenicol and streptomycin were given in succession without apparent effect on the temperature, which fell by lysis between the 6th and 7th day after admission. The fever was often a source of concern to the physicians having care of these infants. They were often reluctant to relate the fever to the scorbutic process, preferring to consider it an indication of some occult infective process.

Hæmorrhagic manifestations occurred in 56% of cases.

The gums were the most common site, but it should be noted that hæmorrhage occurred only where teeth had erupted, the edentulous gum being consistently free of hæmorrhagic lesions. The scorbutic gum was swollen and dark red or purplish in colour, and bled easily. The most striking hæmorrhagic manifestation was a large periorbital effusion of blood giving rise to proptosis and a somewhat alarming appearance. There was no history of trauma in this case. The swelling subsided rapidly once treatment with vitamin C was instituted, and striking improvement was apparent within three days.

X-RAY FINDINGS

The prevalent radiographic findings are shown in Fig. 5.

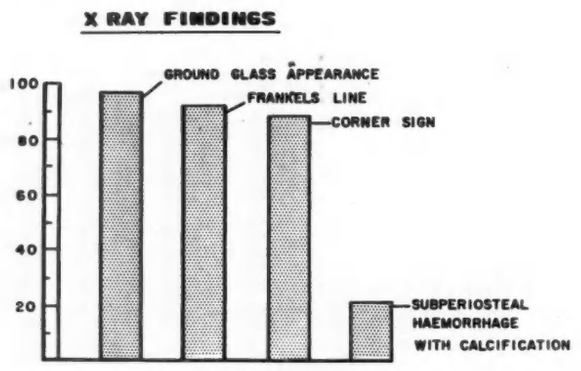

Fig. 5.

No single sign is to be taken as specific for scurvy, each being featured in other disease processes. A combination of two or more of the signs provided evidence of scurvy, to be confirmed by a prompt response to antiscorbutic treatment both clinically and from subsequent x-ray appearance (see Fig. 6).

The "ground glass" appearance is an increased transparency at the end of the shaft with blurring or disappearance of trabecular markings, whilst the cortex of the bone, although thinned, is accentuated relatively to produce a pencilled line effect.

The white line of Frankel is an intensification of the zone of preparatory calcification, the result of a defect in matrix formation without arrest in the process of calcification. This area of calcification is relatively brittle. Deep to it lies the zone of proliferative cartilage, and in scurvy this is the region of greatest trabecular attrition, which juxta-epiphyseal radiolucency is sometimes named the scurvy line.

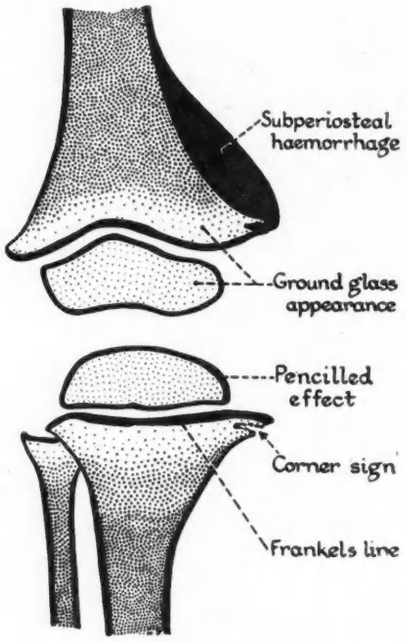

Fig. 6.

The Corner sign is due to subepiphyseal infraction or separation of the epiphysis. Comminution occurs, resulting in mushrooming of the epiphysis on the metaphysis. Provided syphilitic osteochondritis can be excluded, this appearance is almost pathognomonic of scurvy. Sometimes the degree of comminution is greatest in the centre of the end of the bone and this produces a cupping effect, somewhat resembling rickets excepting that the zone of preparatory calcification concave on the cartilage side stands out sharply in scurvy, whereas it is characteristically indistinct and fuzzy in rickets.

BLOOD PICTURE

Anæmia as defined by a hæmoglobin value of 10 g. % or less was present in 19 cases. In two the anæmia was of macrocytic type, one of which had a distinctly megaloblastic marrow pattern. The megaloblastic anæmia responded promptly to treatment with folinic acid as well as vitamin C.

URINALYSIS

An appreciable microhæmaturia was demonstrable in six cases.

DIETARY OBSERVATIONS (see Table V)

TABLE V.—DIET

Breast feeding		no cases
Artificial feeding		33 "
evaporated milk formula used in		30 "
other forms of cow's milk used in		3 "
Milk feeding only with no supplements		4 "
Supplementary feeding		
Cereals offered		16 "
regularly	9 cases	
intermittently or for short periods	2 "	
refused, vomited or not tolerated	5 "	
Other infant foods offered including fruits, vegetables, egg, etc.		9 cases
regularly	4 cases	
refused, vomited or not tolerated	5 "	
Fruit juice offered (orange juice, excepting one given tomato juice)		15 cases
regularly	1 case	
intermittently or for short periods	8 cases	
refused, vomited or not tolerated	6 "	
Cod liver oil offered		2 cases
regularly	2 cases	
Multi-vitamin preparations offered		11 cases
regularly	5 cases	
(in two the preparation was one containing only vitamin A and D).		
intermittently or for short periods	3 cases	
(in 1 case occasional samples from a well-baby clinic).		

Scurvy affected only bottle-fed infants, who with four improbable exceptions had frankly received no supplement whatever of vitamin C or a supplement at once inadequate in amount or inconstant in administration. In the four cases allegedly given an appropriate supplement of vitamin C, there is reason to doubt the accuracy or truthfulness of the dietary history. It is notable that each of the four showed a prompt regression of scorbutic symptoms with vitamin C in ordinary doses. Furthermore a home visit made by a medical student to one of the four families had the following illuminating result: "Mr. H. [the child's father] stated that his wife, upset by the realization that she had not fed the baby food which the doctor questioned her about, told the doctor untruthfully that she had fed the child vitamins and cod liver oil."

TREATMENT

Antiscorbutic treatment, being at the discretion of the physician in charge of the various cases, differed somewhat in form and dosage. Ascorbic acid, in varying dosage from 100 to 1000 mg. daily and given either by mouth or by intramuscular injection, was most commonly prescribed. In three cases, however, it was arranged to give the infant only fresh orange juice as an antiscorbutic in amounts of from 2 to 4 oz. daily. This appeared to be equally effective in providing remission of symptoms. The average time required for definite clinical improvement under treatment was five days.

DISCUSSION

There is evidence of an unusual recent incidence of infantile scurvy in the province of Manitoba. In an effort to determine whether this was representative of a general trend in North America, questionnaires were sent to various pædiatric centres throughout Canada and the U.S.A. requesting information as to the incidence of infantile scurvy during the period 1950 to 1956. The returns received revealed the situation shown in Table VI.

There appears to be no general increase in infantile scurvy on the North American continent. It is unlikely that the increased incidence in Manitoba represents improved case finding, since it is reported from a hospital receiving patients from a fairly constant geographic and social area and provided with pædiatricians of reasonably consistent diagnostic ability. The disease is, furthermore, amongst the most clinically evident, with radiographic means of confirmation long established and readily available. This increased incidence of scurvy nevertheless appears to have met with a lack of clinical awareness on the part of physicians, bearing in mind the frequently incorrect diagnosis made at the time of the infant's referral to hospital.

If a real increase in incidence is accepted, some consideration must be given possible determining

TABLE VI.

Centre	*1950*	*1951*	*1952*	*1953*	*1954*	*1955*	*1956*
Canada:							
St. Paul's Hospital, Saskatoon	2	0	0	0	1	2	0
Children's Hospital, Halifax	8	5	2	4	2	5	2
Hospital for Sick Children, Toronto	7	0	3	4	46	25	
Children's Hospital, Winnipeg	6	0	0	1	14	10	8
U.S.A.:							
Babies Hospital, New York City	0	0	0	0	0	0	0
Bellevue Hospital, New York City	"1 case in past 10 years"						
Children's Hospital, Cincinnati, Ohio	4	2	6	6	3	7	4
Children's Memorial Hospital, Chicago	3	1	3	5	0	0	1
University of Utah Medical School	1	0	0	1	1	0	0
University of Minnesota Medical School	"extremely uncommon during the past three years"						
Fargo, North Dakota	0	0	0	0	0	0	0
Grand Forks, North Dakota	"an occasional case, possibly 1 or 2 per year"						
Colorado General Hospital	0	0	0	0	0	0	0
Medical Center, University of California at Los Angeles						0	0

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factors. The dietary observations make it clear that the giving of inadequate or inconstant supplements of vitamin C to bottle-fed infants occasioned the reported outbreak. A lessened awareness of the need to supplement the diet of bottle-fed infants with vitamin C amongst mothers generally is improbable. An alternative postulate would be that a greater number of infants are bottle fed, and this would be especially valid if the adoption of bottle feeding in place of breast feeding applied to those least likely to appreciate the refinements of artificial feeding or least capable of effecting them.

The trend from breast to bottle feeding has been gathering momentum over the past two or three decades. A possible recent accelerating factor may be the increased incidence of puerperal breast abscess with its discouraging effect on breast feeding. A visit made to St. Anthony's Hospital at The Pas, Manitoba, serves to emphasize this (Table VII) and also the effects of changing traditional feeding habits amongst people ill prepared for or poorly provided with the means to make such a change. The hospital serves a population predominantly Indian or Metis. There were 12 confirmed cases of infantile scurvy (all bottle-fed) during the period 1954 through 1956. There was one death attributable to infantile scurvy.

TABLE VII.—INCIDENCE OF INFANTILE SCURVY AND PUERPERAL BREAST ABSCESS, ST. ANTHONY'S HOSPITAL, THE PAS, MANITOBA

Infantile scurvy		*Puerperal breast abscess*	
1950	no cases	1950	4 cases
1951	no "	1951	3 "
1952	no "	1952	8 "
1953	no "	1953	13 "
1954	5 "	1954	17 "
1955	5 "	1955	10 "
1956	2 "	1956	5 "

The 12 examples of infantile scurvy shown in Table VII were in Indian, half-breed or Metis children (treaty Indians 3, half-breed or Metis 9). It is to be noted that the three Indian children affected were of the Cree tribe, who more readily adopt the white man's ways than do the Chippawans, the other Indian tribe in this area amongst whom breast feeding is almost universal.

A great deal has been written about the advantages of breast feeding, and much lip service has been paid to it by physicians, nurses and other workers in the field of child health, and yet the inescapable signs are of an increasing reliance on artificial feeding methods. In this eventuality some simple means to eradicate infantile scurvy is to be sought. The fortification with vitamin C of evaporated milk, the most commonly used article in artificial feeding, recommends itself. It is generally accepted that the fortification of evaporated milk with vitamin D has gone far to eliminate rickets. The same would surely follow for scurvy if vitamin C could also be included in the practice of fortification of milk products used in infant feeding. It is appreciated that there are greater technical difficulties in achieving antiscorbutic qualities for milk products than existed for antirachitic qualities, because of the relative instability of ascorbic acid. The manufacturers of infant milk products must, however, accept this challenge. In the meantime a return to natural foods as a source of vitamin C rather than reliance on expensive synthetic vitamin concentrates is desirable. It is easier to convince a mother that her bottle-fed infant requires orange or other fresh fruit juice as a source of vitamin C than to imply that some preparation from a drug store is necessary for her infant's well-being.

SUMMARY

Some historical aspects of scurvy in Manitoba are mentioned. A recent outbreak of infantile scurvy in Manitoba is reported. The clinical and radiographic findings are presented and their diagnostic importance related. The dietary factors precipitating scurvy are reviewed, the possible reasons for the reported incidence of scurvy discussed, and means for their prevention indicated.

I wish to acknowledge the advice and encouragement of Dr. Harry Medovy in making this study. The x-ray diagram (Fig. 6) was prepared by the Department of Surgery, University of Manitoba.

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RÉSUMÉ

La première mention du scorbut dans la région qui est maintenant le Manitoba est liée au nom du Danois Jens Munk qui fut forcé d'hiverner dans la rivière Churchill en 1619. Une des plus récentes manifestations de cette avitaminose dans la même province est rapportée ici. On vit le premier cas de cette série à l'Hôpital des enfants de Winnipeg en décembre 1953. Plusieurs autres suivirent. La plupart des enfants étaient agés de 6 à 12 mois. On n'observa aucune prédilection pour l'un ou l'autre sexe, et l'on vit autant de petits malades des régions rurales avoisinantes que de la ville même. Les deux tiers des sujets venaient des classes sociales les moins fortunées. La grande majorité des cas fut référée à l'hôpital sous un diagnostic autre que celui de scorbut.

L'auteur fait le rappel du tableau clinique ainsi que des données du laboratoire et de la radiologie. Le traitement consista indifféremment en jus d'orange ou vitamine synthétique: les résultats furent également bons. On attribue cette avitaminose à l'allaitement artificiel qui prend de plus en plus d'ampleur (le lait de vache est notamment carencé à cet égard). Malgré les difficultés techniques qu'une telle mesure présente, l'auteur suggère un apport artificiel de vitamine C synthétique au lait destiné à l'alimentation des nourrissons.

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OCCULT UTERINE BLEEDING
A DAILY RECORD OF 254 CYCLES

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FRANK SPOTTING of blood and occult bleeding from the uterus at "ovulation time" are described in most textbooks as a normal physiological phenomenon in a vague and small number of women. Occult mid-menstrual bleeding has been intensely studied by Bromberg and Bercovici.[1] Endometrial biopsies were taken by them late in the cycle from 75 women who showed this type of bleeding. All had a secretory type of endometrium. Twelve underwent biopsy on the day of onset of mid-menstrual occult bleeding; all showed secretory endometrium reflecting prior ovulation. Apparently, then, "ovulation bleeding" appears very soon after ovulation. Because there has been no practical method for daily sampling and testing, no clinical use has so far been made of this and other occult uterine bleeding phenomena.

Sturgis[3] states: "The most useful test [for timing of ovulation] should (1) show that ovulation is about to occur or that it has occurred within hours, not days, (2) be easy to perform without complicated and expensive laboratory facilities, and (3) lend itself to interpretation by the patient herself for the purpose of coital timing. Unfortunately, no test at present answers these criteria." To these, one should add: (4) no interference with normal physiology and no barrier to conception.

A simple method for daily testing for occult bleeding was developed, in the hope of finding a test for ovulation time.

Emotions are deeply involved in any effort to pin-point ovulation time. Conscious or even subconscious desires for conception or contraception could easily distort results of a test demanding even simple procedures by patients. To eliminate this variable from this particular study, it was decided not to apply results clinically in any way till they had been summarized and critically reviewed elsewhere. Patients were informed of their own particular patterns only when a pathological lesion or pregnancy was suspected.

For the purpose of this paper, occult intermenstrual bleeding is defined as occult bleeding occurring without the patient's knowledge at least 24 hours after occult blood has disappeared postmenstrually and 24 hours before onset of the next menses.

PROCEDURE

Volunteers were advised not to allow testing to interfere with any of their usual family and marital activities. Those who usually took douches continued to do so. Testing started with the end of obvious menstrual bleeding and continued until the onset of the next flow for three or more consecutive cycles.

Each morning on arising, the patient inserted a vaginal tampon. After 30 minutes, or after getting to work, she removed it by the distal string and immediately dropped it, cervix end first, into a specially made polyethylene envelope. The envelope's open end was folded twice and fixed with two large paper clips. Her name and day of cycle were written on a special roughened area on the envelope. The latter was then placed in a paper mailing envelope and posted, if possible, the same day. The vaginal contents on the tampon, therefore, had not in any way been contaminated. In the suburbs some samples had to be mailed a week at a time, and some came from as far away as New York, Quebec City, the DEW line and Toronto.

Twelve envelopes were processed at a time. The time lapse from postmark to testing was recorded, as were the presence of bloodstain, moisture or discoloration. The sealed end of the polyethylene envelope was ligated with a twisted, small elastic band one inch from that end to trap the secretions at the cervix end of the tampon. This allowed the other end to be used as a clean handle. The bunched end of the envelope was then cut in a convex curve with curved surgical scissors, avoiding the tampon. The polyethylene is self-sealing and self-cleaning. A sharp squeeze made the test end available and it was placed on the mailing envelope. Four drops of distilled water were dropped on to the tampon and two minutes allowed for solution of any available contents. The tampon's tip was then firmly touched to two pieces of filter paper and the paper tested for pH and then occult blood in concentrations of 1 in 10,000 and 1 in 100,000. Readings were done simultaneously exactly two minutes later with one glance. No prolonged searching was allowed. The technicians had no access to the master record or previous patterns. (The fixation of female technicians on day 14 of the cycle must be overcome.) The results were coded and tabulated blindly in another location by other technicians.

Tampax ® vaginal tampons were used. The cardboard paper case and plunger allowed insertion, sampling and testing without any possible contamination.

Vaginal tampons have already been proven innocuous by Karnaky,[6] who reported on 100 women who inserted them twice daily continuously for six months; there were no changes in bacterial flora, pH, glycogen content, and cervical or vaginal mucous membrane.

The cotton alone will not oxidize hæmoglobin. Tests on clean tampons gave no positive results with the reagents used. Single drops of blood

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allowed to dry on the tip gave positive tests for occult blood in the manner described as long as a month after application. The test tampon also removed accumulated debris, leaving the vagina clear for the next day's discharge. This gave very sharply defined results.

Hematest® and Occultest® test tablets were used for determining the presence of hæmoglobin in concentrations of 1 in 10,000 and 1 in 100,000 respectively. The test reaction depends basically on the oxidation of dissolved hæmoglobin to a blue dye by orthotoluidine in less than two minutes. A blue colour appearing in more than two minutes is due to other organic material present. Small amounts of blood in the vagina lose their hæmoglobin in 48 hours or less through oxidation by vaginal bacteria and enzymes.

MATERIAL

Eighty healthy volunteers from private practice between the ages of 20 and 40 mailed in daily tampons for three or more cycles, and some are continuing to do so indefinitely. Each of these women had had within the previous two years a complete history, physical examination, chest radiograph, Wassermann test, hæmoglobin test, blood sugar, sedimentation rate, urinalysis (including occult blood), pelvic examination and endocervical biopsy by the Nolan-Budd technique.[7] Papanicolaou smears were examined when available. No procedures for purely research purposes were performed at any time.

Forty-eight hundred tampons were tested. In an effort to obtain parallel confirming data, over 2000 tests for pH were performed to reflect changes in cervical mucus. They were of no clinical value. It was soon obvious that the time lapse from sampling to testing was not important. Two hundred tampons and their envelopes were examined by a variety of methods in an attempt to obtain parallel endocervical mucous fern tests. This was possible only twice, and the procedure was dropped. Sealed dry tampons were sent for cytological examination but the slides, though skilfully made, were not satisfactory because of dehydration of cells. A parallel cytological study would have been ideal.

A specially trained nurse contacted each patient twice during each cycle and took a detailed gynæcological history of that particular cycle with particular emphasis laid on douching, leukorrhœa, "ovulation pain", "ovulation bleeding", premenstrual tension and dysmenorrhœa. Each phenomenon or complaint was charted parallel with the tests and day of cycle. No questions about intercourse were asked.

RESULTS

A total of 254 cycles have so far (December 15, 1957) been recorded on 80 patients (Table I), with a maximum of four cycles per patient and an average of three. A sharply defined episode of occult intermenstrual vaginal bleeding was found in 118 cycles using a sensitivity test of 1 in 10,000 and in 30 more with a sensitivity of 1 in 100,000 (Table IV, Pattern A). The use of both tests simultaneously gave a rough quantitative pattern. Persistent occult bleeding, after the menses had apparently finished, occurred in 15 cycles (Table IV, Pattern B). A single bloodstained tampon in the intermenstrual period with no history of frank bleeding was noticed in 14 cycles. Thirty-six cycles had to be eliminated from appraisal because one or two tampons only had been omitted.

TABLE I.—OCCULT MID-MENSTRUAL BLEEDING

A. Single episode, sharply defined: 1/10,000	118 cycles
B. Confluent postmenstrual episodes	32 "
C. Two isolated episodes in same cycle	43 "
D. Confluent premenstrual episodes	14 "
E. No occult bleeding even at 1/100,000	32 "
F. Conception during test period	9 cases
G. Tubal pregnancy	1 case
H. Multiple episodes or continuous bleeding	19 cycles

Continuous daily positive results were found in only eight cases for 19 cycles. Two of these have large uteri containing fibroids, which are asymptomatic with no frank metrorrhagia. Three had no demonstrable lesions but had been treated for iron-deficiency anæmia for years. Another patient who later developed severe menorrhagia and metrorrhagia was found to have a large endometrial polyp. Frank abnormal bleeding was preceded by occult bleeding in two cases by at least a month. In the last two of this group there is no complaint, no anæmia and no disease. The long-term follow-up of these eight women will be very important. Further procedures are not as yet justifiable.

Twenty-four cycles in eight women with a long-standing history of sterility did not show one single positive test (Table IV, Pattern E). Two of these have been shown radiologically to have bilateral tubal hydrosalpinx. The only other cases in the whole series with persistently negative cycles are a childless women of 21, married two years, and a 35-year-old healthy mother of two. In seven different women single negative cycles appeared before or after "double episodes" (see below).

Seven sterile women with proven secretory endometrium and tubes proven patent on x-ray examination all showed isolated occult bleeding in the intermenstrual period.

Occult intermenstrual bleeding commenced anywhere between the 7th and 20th day in women with cycles of 30 days or less (Table II). It commenced as late as the 25th day in women with longer cycles and on the 32nd day of a 65-day cycle. Consecutive cycles usually revealed patterns peculiar in degree and duration to that particular patient, but the day of onset varied by as much as five days in many and by more than that in a few.

A second distinct episode of occult bleeding occurred about a week later in the cycle 43 times

TABLE II.—DAY OF ONSET OF INTERMENSTRUAL OCCULT BLEEDING 1/10,000

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
						x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x			
						x	x	x	x	x	x	x	x	x	x	x	x	x			x		x				
							x	x	x	x	x	x	x	x	x	x	x	x									
							x	x	x	x	x	x	x	x	x	x	x	x									
							x	x	x	x	x	x	x	x	x	x	x										
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in 26 women (Table III). In these women it recurred with the same periodicity and volume in other cycles. In 7 cases adjacent cycles were completely negative. This second episode was usually more prolonged than the first (Table IV, Pattern C). Occasionally both episodes merged.

Nine pregnancies occurred in the 60 fertile women during daily testing, in one of the first three cycles, and testing continued daily for as long as 55 days. All of these showed isolated early occult bleeding episodes. In all but one of these, occult bleeding reappeared 6 to 9 days after its first appearance and continued intermittently

DISCUSSION

The method described has proven in a large series to be a practical method of determining the presence from day to day of uterine occult bleeding. Any of the accepted tests for hæmoglobin could have been used. An intelligent assistant can perform 300 or more of these tests a day. Nursing or laboratory training is unnecessary. Clinical assessment through three cycles will pick out a definite pattern of bleeding. We must remember that any of the known causes of metrorrhagia can arise and cause occult intermenstrual bleeding. Intermenstrual occult blood related to ovulation

TABLE III.—DAY OF ONSET OF SECOND EPISODE OF OCCULT BLEEDING

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
												x	x	x	x	x	x	x	x	x	x	x		x			
												x			x	x	x	x	x	x	x	x					
															x	x	x	x	x	x	x	x					
															x	x	x	x	x	x	x	x					
																		x	x	x							
																		x	x	x							
																			x								

while the patients were under observation. There were no abortions. A patient with a history of one previous tubal pregnancy developed another tubal pregnancy in the 3rd test cycle. In this case occult bleeding appeared on the 12th day and recurred on the 17th day. Frank spotting and pain were first noticed on the 23rd day of the cycle. Occult intermenstrual bleeding was recorded in 89.4% of cycles of all fertile women and in all cycles of all those with radiologically proven patency of fallopian tubes.

In 14 cycles another episode of occult bleeding preceded the onset of menses by 2-4 days and merged with it (Table IV, Pattern D). In 74 cycles occult bleeding at 1/10,000 occurred only on one day during the entire intermenstrual period and the absence of a single tampon would have given the appearance of a negative cycle.

The results obtained are identical in pattern, but not in timing, with those obtained by Bromberg and Bercovici. Their experience with sterility problems is identical.

apparently appears at the cervix a few hours after ovulation if the tubes are open, and apparently comes from the ovary. Twelve hours later the ovum should be dead and conception impossible. If the occult bleeding found does coincide with ovulation, the timing obtained proves that the ovary does not (as we have been taught) punch a clock or count days from either end of the cycle. Prediction of ovulation time would be possible only in the presence of a proven constant pattern, and the latter is not common. Accurate timing will demand continual testing of many cycles and then monthly testing in the few days indicated. Complete absence of positive tests would, on these data, imply sterility.

Three thousand tampons were tested directly without transfer to paper. These all showed positive tests on the same days as the above. In addition they were positive on many other days. The episodes above were all associated with positive tampons, but many completely unrelated tampons were also positive. Reducing the distilled

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TABLE IV.—OCCULT INTERMENSTRUAL UTERINE BLEEDING

Day of cycle	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*	*20*	*21*	*22*	*23*	*24*	*25*	*26*	*27*	*28*	*29*	*30*
																Pattern A														
Case 70, cycle 3																														
Bloodstain on tampon..	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M					
Occult blood 1/10,000...	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	X	–	–	–	–	–	–	–	–	M					
Occult blood 1/100,000..	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	X	–	–	–	–	–	–	–	–	M					
																Pattern B														
Case 73, cycle 1																														
Bloodstain on tampon..	M	M	M	M	M	M	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M
Occult blood 1/10,000...	M	M	M	M	M	M	X	X	X	X	X	–	–	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M
Occult blood 1/100,000..	M	M	M	M	M	M	X	X	X	X	X	–	–	X	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M
																Pattern C														
Case 65, cycle 2																														
Bloodstain on tampon..	M	M	M	M	M	M	–	–	–	–	–	–	–	–	–	–	–	–	–	X	–	–	–	–	–	–	–	–	–	M
Occult blood 1/10,000...	M	M	M	M	M	M	–	–	–	–	X	–	–	–	–	–	–	–	–	X	–	–	–	–	–	–	–	–	–	M
Occult blood 1/100,000..	M	M	M	M	M	M	X	–	–	–	X	–	–	–	–	X	–	–	X	X	X	X	–	–	–	–	–	–	–	M
																Pattern D														
Case 80, cycle 2																														
Bloodstain on tampon..	M	M	M	M	M	M	M	–	–	–	–	–	–	–	–	–	X	–	–	–	–	–	–	–	–	–	M			
Occult blood 1/10,000...	M	M	M	M	M	M	M	–	–	–	–	–	–	–	–	–	X	–	–	–	–	–	X	X	X	X	M			
Occult blood 1/100,000..	M	M	M	M	M	M	M	–	–	–	–	–	–	–	–	X	X	X	–	–	–	X	X	X	X	X	M			
																Pattern E														
Case 5, cycle 1																*Daily leukorrhœa*														
Bloodstain on tampon..	M	M	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M
Occult blood 1/10,000...	M	M	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M
Occult blood 1/100,000..	M	M	M	M	M	M	M	X	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	M

X = Positive test – = Negative test M = menses.

water to one drop and testing only the very tip of the tampon gave a closer but not complete correlation. The sides of the tampon gave many more positives. Removal of the dry tampon in the intermenstrual period might therefore have an invisible abrasive effect in some patients. No lesions were ever seen on examination of the mucosa. Lubrication was not advisable in this search for a normal pattern, as this procedure adds a strong potential variable to our test.

The patterns of bleeding are varied in duration and quantity, but were uniform in type for each patient. Their interpretation easily lends itself to a free flow of physiological fantasy. Evidence to suggest that occult bleeding at ovulation comes from the ruptured graafian follicle and corpus luteum and not the endometrium fits our present knowledge of corpus luteum and fallopian tube physiology. Sturgis[3] has already suggested this possibility. Seven patients have had a hysterosalpingography, which showed normal fallopian tubes. All of these have secretory endometrium. All showed apparent ovulation bleeding. Two patients with radiologically proven closed tubes, secretory endometrium and sterility had not one single positive test in seven cycles. Corner[4] describes almost daily intracavitary bleeding in the corpus luteum from ovulation to the onset of menses. Escape of this blood could explain the prolonged late patterns found by myself and by Bromberg and Bercovici. Biopsy of bleeding ruptured ovaries which have demanded laparotomy always shows a well-developed corpus luteum. Minor similar episodes must occur very often with delivery of the blood via the tubes to the cervix. No bleeding lesions of human endometrium at this time have even been demonstrated. If patients with normal ovaries who need laparotomy, were operated on at the onset of "occult intermenstrual bleeding" much could be learned.

The second possibility, never previously discussed, is that the second distinct occult episode is from a second ovulation in the same cycle. The topic of double ovulation has been avoided in all studies of ovulation timing. It must, however, occur for the conception of non-identical twins.* Further research along this line is certainly indicated.

The finding of a persistent positive pattern as first described by Rachel Stein-Werblowsky[5] should lead to the discovery of early ulcerative lesions of both a benign and malignant nature. This finding should always precede frank abnormal bleeding for varying periods. In areas where facilities for cancer screening by cytological methods are absent or limited, the mailing method described could be be used as a preliminary screening or follow-up procedure. It will not diagnose possible premalignant lesions. Four women with mild basal cell hyperplasia and four with marked endocervical squamous metaplasia showed normal patterns. Carcinoma *in situ* should not cause abnormal bleeding. Persistent leukorrhœa in the absence of ulcerative lesions did not cause positive tests. Constant leukorrhœa was present in some of the women with completely negative cycles. It was, however, present in all of those with daily positive cycles. Douches had no effect on the patterns obtained.

*Suggestion by Dr. S. Kronick of Ottawa.

The continuous occult bleeding found in all of the 9 cases of pregnancy has not been described before. Its onset coincides with the expected time of implantation of the trophoblast. Hurtig *et al.*[7] describe gross hæmorrhage about the implanted ovum by the 11th day after conception. Persistent loss of microscopic amounts of blood from the periphery of the placenta is certainly possible. Perhaps this continued occult blood loss is a factor in the cause of some anæmia of pregnancy.

The only variables possible in this test are the depth and duration of insertion of the tampons.

SUMMARY AND CONCLUSIONS

In an attempt to detect ovulation time by testing for intermenstrual occult bleeding from the uterus, many new phenomena have been detected and new problems have arisen.

A reliable practical method of daily testing for uterine occult bleeding has been developed and tested through 254 cycles on 80 apparently healthy women. A preliminary report is given on the data obtained. Occult intermenstrual uterine bleeding can be used to study ovulation time, sterility, early ulcerative lesions, bleeding corpus luteum, nidation of the fertilized ovum, ectopic pregnancy, iron-deficiency anæmia and anæmia of pregnancy.

The method used will definitely not prevent conception or interfere with pregnancy.

Occult intermenstrual bleeding, when associated with ovulation, apparently comes from the ovary and follows by hours, rupture of the graafian follicle; however, more convincing proof of this is needed. The day of onset of such bleeding could be used to time laparotomy or culdoscopy for other reasons for conclusive proof of this theory.

The potential clinical applications of this procedure are many and extremely important. It most certainly should not be used for detection of safe periods until this series has been reduplicated elswhere. A much larger number of complete cycles needs to be recorded. Further proof of the exact time relation between rupture of the follicle and the onset of occult intermenstrual bleeding is needed. Until then it could be used to help time coitus in sterile healthy couples. The concept of possible double ovulation in the same cycle needs investigation and must be remembered.

The vaginal tampon is not a perfect "collector" for occult blood but is the best we have for the purpose.

After careful clinical appraisal, intelligent women could easily be taught to test themselves at home for occult blood and mail in only the reports of tests.

This trial would not have been possible without the cooperation of the 80 private patients who volunteered to help by submitting material daily for three months and more. The project was made possible by a grant from Canadian Tampax Corporation, Ltd. The Ames Co. supplied Hematest and Occultest tablets. Florence Hurtig charted all the results. I would like to thank them all.

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THE ADVANTAGES OF COBALT^{58} TAGGED VITAMIN B_{12} IN THE STUDY OF VITAMIN B_{12} ABSORPTION*

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DURING THE PAST six years, radioactive vitamin B_{12} absorption tests have been used extensively in the study of megaloblastic anæmias.[1-5] A better understanding of the absorption, metabolism, storage and excretion of vitamin B_{12} has been made possible by the use of these techniques. Moreover, the absorption defect in case of pernicious anæmia can be demonstrated even though the anæmia has been corrected by treatment. These new techniques are useful to the clinician as well as to the research worker.

The possible danger of prolonged irradiation has caused some concern. Cobalt^{60} has a physical half-life of more than five years and it is this isotope which has been employed in most reported studies. We have used vitamin B_{12} tagged with cobalt^{58} in an attempt to minimize the radiation hazard. Cobalt^{58} has a half-life of only 72 days. We have studied the counting properties of cobalt^{58} and have used a modified Schilling technique to determine its clinical usefulness.

COUNTING PROPERTIES

Two 5-ml. counting samples were prepared. One contained 0.05 μc. of cobalt^{58} and one contained 0.05 μc. of cobalt^{60}. The counting properties of the two samples were compared using both integral and differential counting techniques. The results of counting the 0.05 μc. samples of cobalt^{58} and cobalt^{60} using the

*From the McGill University Clinic of the Montreal General Hospital.
Presented at the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, October 18, 1957.

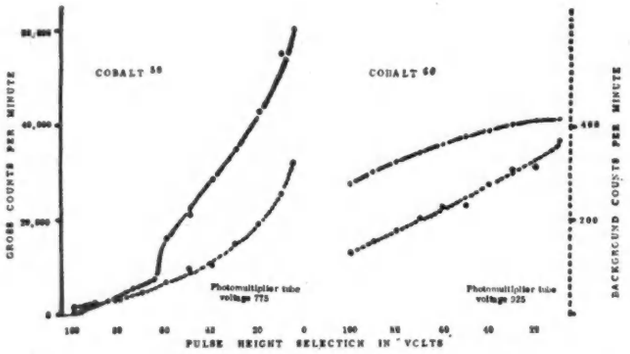

Fig. 1.—Integral counting of 0.05 microcurie samples of cobalt^{58} and cobalt^{60}.

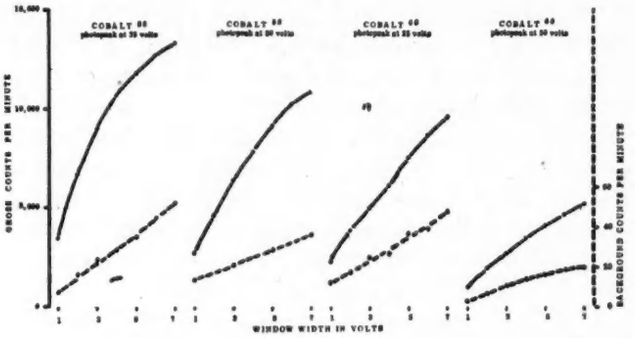

Fig. 2.—Differential counting of 0.5 microcurie samples of cobalt^{58} and cobalt^{60}.

integral technique are shown in Fig. 1. More counts were obtained from the cobalt^{58} sample. With a similar background of 150 counts per minute (c.p.m.), approximately 35,000 gross c.p.m. were obtained from the cobalt^{58} sample and 30,000 from the cobalt^{60} sample. The gross and background counts obtained when the same two samples were counted using the differential technique are shown in Fig. 2. Again, with similar background levels more counts per minute were obtained from the cobalt^{58} sample than from the cobalt^{60} sample. For example, at the 25 volt photopeak, with a background of 30 c.p.m., cobalt^{58} gave a gross count of about 12,000 c.p.m. while cobalt^{60} gave only 7000 gross c.p.m.

Preliminary calculations suggested that the radiation hazard from 1.0 μc. of cobalt^{58} tagged vitamin B_{12} would be no greater than the hazard from 0.25 μc. of cobalt^{60} tagged vitamin B_{12}. This latter dose is the one most commonly used. Consequently two further 5-ml. test samples were prepared. The radioactivity of one (50 $\mu\mu$c.) simulated the unconcentrated urine radioactivity from a patient with pernicious anæmia given 1.0 μc. of cobalt^{58} tagged vitamin B_{12} by mouth in a Schilling test. The radioactivity of the other (12.5 $\mu\mu$c.) simulated the unconcentrated urine radioactivity from a patient with pernicious anæmia given 0.25 μc. of cobalt^{60} tagged vitamin B_{12}. Again, the counting properties of the two isotopes were compared using integral and differential techniques.

The results obtained by differential counting of the second two specimens containing 50 $\mu\mu$c. of cobalt^{58} and 12.5 $\mu\mu$c. of cobalt^{60} are shown in Fig. 3. In ten minutes' counting time, the cobalt^{58} sample gave a gross count of 520 against a background of 340, yielding 180 net counts. This amounted to 18 c.p.m. (S.D. 3). These data suggested that the degree of counting accuracy would suffice for a modified Schilling test using 1.0 μc. of cobalt^{58} tagged vitamin B_{12} without recourse to urine concentration in cases of pernicious anæmia. In a similar counting period the cobalt^{60} sample gave a gross count of 180 against a background of 160, yielding 20 net counts. This amounted to 2 c.p.m. (S.D. 1.8). These data suggested that the degree of counting accuracy would not suffice for a modified Schilling test using 0.25 μc. of cobalt^{60} tagged vitamin B_{12} without recourse to urine concentration in cases of pernicious anæmia.

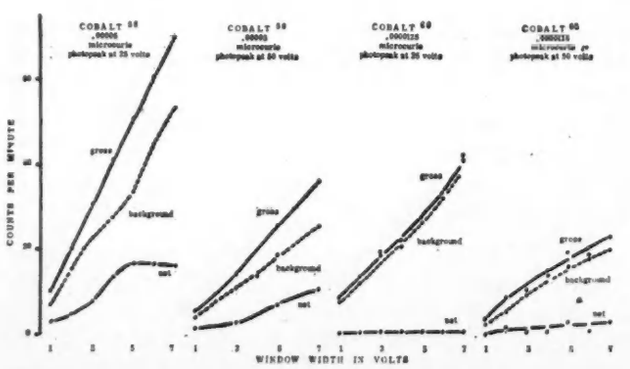

Fig. 3.—Differential counting of low activity samples of cobalt^{58} and cobalt^{60}.

CLINICAL USE

The clinical trial of vitamin B_{12} tagged with cobalt^{58} was performed using a modified Schilling technique. A 0.5-μg. dose of vitamin B_{12} tagged with 0.4 to 1.2 μc. of cobalt^{58} was administered to fasting patients. One hour later a large flushing dose of 1000 μg. of crystalline vitamin B_{12} was given by intramuscular injection. The 24-hour urine radioactivity was compared with the radioactivity of the orally administered dose.

Forty-four patients were studied. Fifteen persons free of hæmatologic, gastro-intestinal and renal disease served as controls. Thirteen patients with pernicious anæmia in remission, six patients with pernicious anæmia in relapse, and three patients with intestinal malabsorption of the idiopathic type or resulting from small bowel surgery were studied. In addition, we studied three patients after subtotal gastrectomy and four patients with gastric achlorhydria who showed no evidence of hæmatologic disease.

The results of the clinical trial are shown in Fig. 4. The data are expressed as the percentage of the oral dose excreted in the urine in a period of 24 hours. Normal values ranged from 17.5% to 46% with a mean value of 27% (S.D. 8.4). In patients with pernicious anæmia the values ranged from 0.54% to 5.8% with a mean value of 2.0% (S.D. 1.2). There was no overlap between these two groups. The results are less clear-cut in the other three groups. The values in one of the three patients with intestinal malabsorption fell in the pernicious anæmia range (2%). In the other two, values (6%, 13%) were somewhat higher but still below the normal range. One patient who had undergone subtotal gastrectomy was in the per-

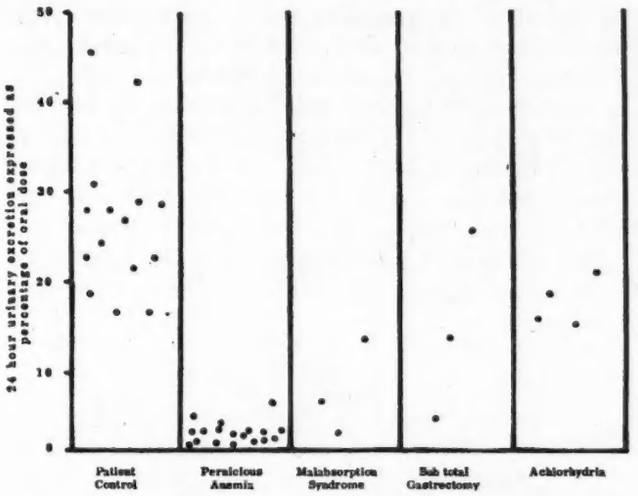

Fig. 4.—Scattergraph showing the results of B_{12} absorption studies using a modified Schilling technique.

nicious anæmia range (3%). One (25%) was in the normal range and the third (13%) fell between these values. The four patients with gastric achlorhydria showed values (14%, 16%, 18%, 20%) close to the normal range.

The counting accuracy of unconcentrated urine samples permitted a clear differentiation between normal persons and patients with pernicious anæmia when 1.0 μc. of cobalt^{58} tagged vitamin B_{12} was used as the test dose.

DISCUSSION

The calculation of the quantity of radiation delivered from internally administered radioisotopes is a problem of great complexity. The decay scheme of the isotope, the type and energy levels of the emissions, and the distribution of the isotope throughout the body, as well as the biological half-life, must be known. The type and energy levels of the emissions from cobalt^{58} and cobalt^{60} are known.[7] However, far less is understood about the biological half-life of vitamin B_{12} and its distribution within the body. Substantial quantities of cobalt^{60} tagged vitamin B_{12} remain in the liver for more than six months.[5] It is a reasonable assumption that the biological half-life of cobalt incorporated in vitamin B_{12} is at least six months. The maximum permissible body load is about 7.2 μc. for cobalt^{58} and 3 μc. for cobalt^{60}.[7, 8] Assuming a biological half-life of six months for the cobalt incorporated in vitamin B_{12}, less radiation is delivered to the liver from 1.0 μc. of cobalt^{58} tagged vitamin B_{12} than from 0.25 μc. of cobalt^{60} tagged vitamin B_{12}. Should the biological half-life exceed six months, the advantage of the short-lived isotope, cobalt^{58}, would be increased. The dose of cobalt^{58} used in tagged vitamin B_{12} in our clinical studies is far below the maximum permissible body load.

The counting accuracy of unconcentrated urine samples permitted a clear differentiation between normal individuals and patients with pernicious anæmia when 1.0 μc. of cobalt^{58} in tagged vitamin B_{12} was used as the test dose.

SUMMARY

The counting properties of cobalt^{58} are superior to those of cobalt^{60}.

In using tagged vitamin B_{12} the radiation hazard from 1.0 μc. of cobalt^{58} is less than the hazard from 0.25 μc. of cobalt^{60}.

An oral dose of 1.0 μc. of cobalt^{58} tagged vitamin B_{12} was used for a modified Schilling test. Satisfactory results were obtained in normal individuals and patients with pernicious anæmia without recourse to urine concentration.

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RÉSUMÉ

La plupart des expériences sur le métabolisme de la vitamine B_{12} ont été faites à l'aide de cobalamine marquée au Co^{60}. Or cet isotope a une période de plus de cinq ans et comme tel, présente certains dangers de radiations non négligeables. Les auteurs de cet article ont entrepris de réaliser leurs expériences dans ce domaine à l'aide de vitamine B_{12} marquée au Co^{58}, dont la période n'est que de 72 jours. De plus, le spectre d'émission de ce dernier isotope offre l'avantage d'un meilleur enregistrement que l'autre dans les compteurs à scintillations. On a donc pu administrer aux malades des doses de l'ordre de 1.0 μc tout en restant dans les limites de la sécurité, alors que la dose acceptée de Co^{60} dans ces circonstances est de 0.25 μc.

EFFECTS OF ISONIAZID PROPHYLAXIS

In a study by Palitz (*Am. Rev. Tuberc.*, 77: 232, 1958), isoniazid chemoprophylaxis in a continuous dosage of 10 mg./kg./day reduced the size of the local reaction, decreased the incidence of ulceration, and exerted a significant suppressive effect on the level of tuberculous allergy following the introduction in adult humans of an average immunizing dose of BCG vaccine. This suggests that the multiplication of living cells is altered by isoniazid chemoprophylaxis under these conditions. Nevertheless, 80% of the drug-treated subjects in the experiment developed tuberculin hypersensitivity as revealed by responses to 1.0 mg. of tuberculin. Suppressive effects of the same order were noted when the drug was stopped at the time of BCG vaccine inoculation and resumed after 18 days.

In the drug-treated, BCG vaccine-inoculated groups, allergy levels were maintained with relatively little loss (several actually gained allergy) after withdrawal of the drug, in contrast to the large loss of hypersensitivity in the group which had not received the drug. It is possible that renewed multiplication of BCG cells was responsible for the individual gains in allergy. The remarkable ability of an attenuated organism such as BCG to "persist" under strong drug attack is noted.

The author feels that *BCG vaccine would be especially useful in combination with chemoprophylaxis* since allergy and immunity develop under this combined therapy. The immunizing vaccine could be either a standard dose of isoniazid-resistant organisms or a somewhat larger dose of isoniazid-susceptible bacteria. The protection provided by the vaccine a few months after inoculation would, of course, be of a different nature from that provided by chemoprophylaxis. It is the result of the sensitizing and immunizing properties of the vaccine, and once inoculated, provides varying degrees of protection, probably for years.

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THE "HIGH" DEFECT IN THE ATRIAL SEPTUM

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THE SPECTACULAR advances in heart surgery have brought into prominence several hitherto unappreciated anomalies of the atrial septum and the pulmonary veins. One that has given much trouble is a "high" septal defect—a foramen in the atrial septum close to the entrance of the superior vena cava, between the vein and the fossa ovale.

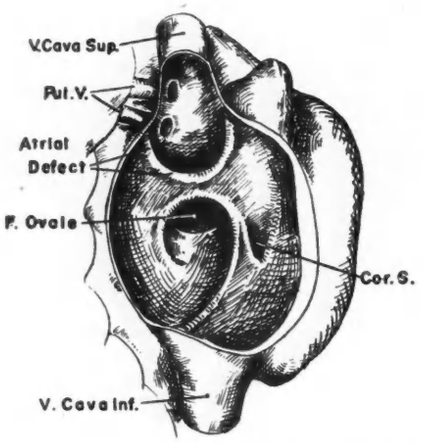

Fig. 1.—High defect in the atrial septum combined with the more usual patent foramen ovale. After Lewis *et al.*[2]

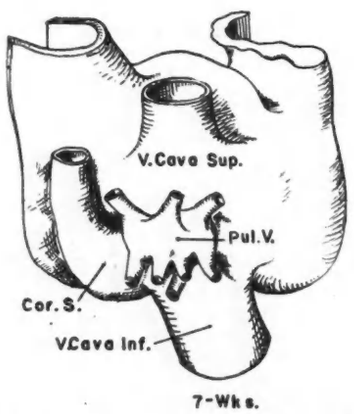

Fig. 2.—Wax model of pulmonary veins entering atria of a 15-mm. human embryo. ×35.

The defect, placed so near the orifice of the right superior pulmonary vein or veins, permits a diversion of pulmonary blood into the right atrium and even a shift of the vein itself to the right side of the heart. Watkins and Gross[1] find high septal defects in 15 out of 43 cases operated on for atrial septal abnormalities. Lewis *et al.*[2] describe several combinations of the high septal defect with a patent foramen ovale; one of their figures is reproduced as Fig. 1.

The high septal defect is a hazard for the surgeon; it also poses a problem for the embryologist. Such a foramen is not a normal episode in human development as are the other foramina of the atrial septum. The usual explanation of the high septal defect attributes it to a chance combination of an excessive degeneration of atrial septum I with an incomplete development of the upper part of atrial septum II. Patten[3] has shown that septum I may almost disappear; Odgers[4] points out that the upper part of septum II is a distinct and rather variable entity. Should both septa misbehave, an unusual foramen would result, which would give the right superior pulmonary vein access to the right atrium. Another explanation has been advanced by Hudson[5] and Ross.[6] They trace the high septal defect to a persisting leftward extension of the sinus venosus, into which an anomalous pulmonary vein has previously entered.

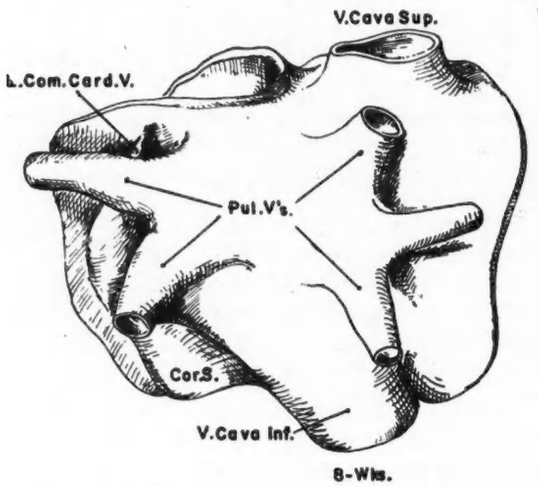

Fig. 3.—Wax model of pulmonary veins of a 29-mm. human embryo. ×35.

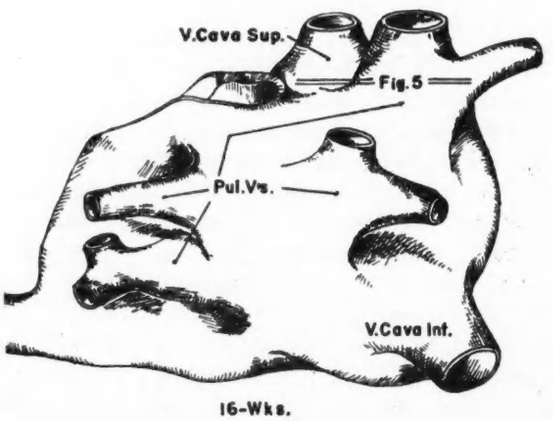

Fig. 4.—Wax model of pulmonary veins of a 130-mm. human embryo. ×17.

A simpler explanation occurred to me while making a series of student models of the later stages of the development of the pulmonary veins. The pulmonary veins migrate considerably as they develop; the terminal segments of the right superior pulmonary vein and the superior vena cava come to lie so close together as to have a common muscular wall between them. A fistula in this common wall could produce the high septal defect.

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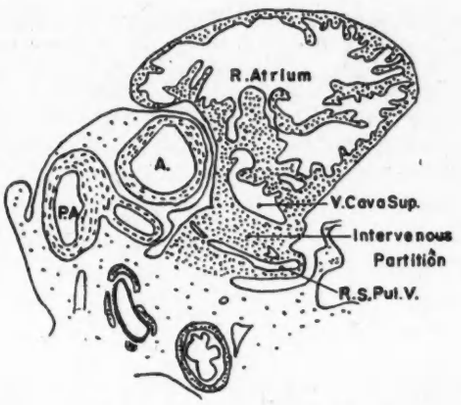

Fig. 5.—Section through right superior pulmonary vein and vena cava superior of a 130-mm. embryo heart at the level marked in Fig. 4. ×5.

A brief account of the later development of the pulmonary veins is here in order, for such details are not given in standard textbooks. According to Aüer,[7] the human pulmonary veins appear in the 2-mm. embryo as a single capillary tap, whose branches drain both lung buds and the adjacent gut. The orifice of the primitive single vein is low down in the left atrium, close to the atrioventricular valve cushions and just to the left of the growing edge of atrial septum I. The orifice of the single pulmonary vein lies close also to the entrance of the left common cardinal vein (the future coronary sinus) and to that of the inferior vena cava.

Beginning with the seventh week, the capillary-like common pulmonary vein expands into a wide and shallow recess (Fig. 2), which receives the former branches of the vein, by now independent vessels. An additional twig from the œsophagus is not unusual.

The primitive arrangement of the pulmonary veins is soon disturbed by a profound rearrangement of the chest organs. The heart migrates downward; in man and the anthropoid apes its apex swerves to the left. The lungs, originally placed below the heart, move upward and envelop it. The terminations of the separate pulmonary veins are naturally affected; they shift upwards and laterally over the atrial walls (Figs. 3 and 4). The left pulmonary veins are at first hindered by the remnant of the left common cardinal vein, but with its further degeneration they are free to migrate. The orifices of the right veins lie against the atrial septum, which restricts their lateral movement; in consequence their migration is mainly upward. When the right superior pulmonary vein comes to rest, it runs across the lowest part of the superior vena cava and opens into the left atrium close to the atrial septum (Fig. 4). The recess derived from the primitive pulmonary vein becomes a broad depressed area which is added to the left atrium.

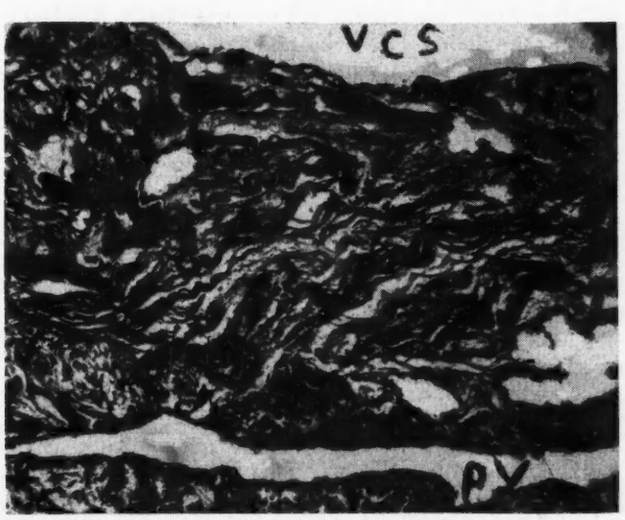

Fig. 6.—Photomicrograph of the intervenous partition between the right superior pulmonary vein and the vena cava superior shown in Fig. 5. ×60.

As a result of these changes, the terminal segments of the right superior pulmonary vein and the superior vena cava acquire a peculiar relation to each other during midfetal life. Where the two veins come in contact, the adjacent vessel walls fuse into a common muscular partition (Figs. 4, 5 and 6, from a 130-mm. embryo) which continues without demarcation into the atrial septum. This intervenous partition is loose-textured, spongy, and permeated by blood-filled spaces (Fig. 6). In still older embryos the partition is thinner and more compact; in adult hearts it is again divided in varying degrees.

Such a spongy muscular partition resembles very much the early ventricular septum. Just as the ventricular septum is occasionally perforated by abnormal foramina, so the partition between the two veins might be broken through and the high septal defect created. Such a defect initially would connect the two veins only, but once established would be free to expand downward into the true atrial septum and even to coalesce with a patent foramen ovale, as Lewis *et al.* have found.

Add to this some absorption of the stem of the right pulmonary vein and a slight migration of its primary branches, and the condition of affairs in Fig. 1 would be attained.

SUMMARY

The author suggests that the high atrial septal defect is an abnormal foramen made possible by the migration of the right superior pulmonary vein, whereby it comes to lie across the superior vena cava and is fused to it. Perforations in the common muscle wall could produce a high septal defect. Such a defect is at first above the true atrial septum, but can secondarily expand into it. Analogous foramina do occur in the ventricular septum.

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RÉSUMÉ

Contrairement aux autres défauts du cloisonnement inter-auriculaire, comme le trou de Botal, par exemple, les défauts d'oblitération du sommet de la cloison ne correspondent à aucun stage de développement embryonnaire humain. Ces anomalies de la partie haute du septum seraient le résultat de la migration de la veine pulmonaire supérieure droite qui vient se poser en travers de la veine cave supérieure et se joint à elle. Toute perforation de la paroi musculaire commune aux deux veines peut donner lieu à une communication inter-auriculaire située d'abord au-dessus de la paroi même mais qui peut, par la suite, venir à l'inclure. De semblables foramina peuvent se produire dans la paroi inter-ventriculaire.

LOSS OF SURGICAL NEEDLES DURING TONSILLECTOMY*

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THE LOSING of a surgical needle or its broken fragment during tonsillectomy belongs to the same category of hazards as the aspiration of a sponge, a broken anæsthesia needle, or tooth, with such serious implications as to make tonsillectomy anything but a "minor operation".

The dangers of losing a surgical needle in the throat, the difficulty and uncertainty of its recovery, and the liability for malpractice are just cause for the greatest concern to the surgeon and contribute to the importance of this problem.

INCIDENCE

Although reports on loss of surgical needles during tonsillectomy are few, this harrowing accident occurs more frequently than is reported, probably because of reluctance to broadcast mishaps. In fact, it is not an uncommon accident and is more frequently encountered among general practitioners, simply because they remove most of the tonsils.

It is not so infrequent in the experience of otolaryngologists either: of 65 returned questionnaires sent out by Weiss[1] to 180 otolaryngologists in 1941, 34 reported a total of 67 broken needles (57 suture needles and 10 local anæsthesia needles) lost during tonsillectomy, and the number of accidents reported by any one specialist ranged from one to six.

At a meeting of the Section of Otolaryngology of the American College of Surgeons in Philadelphia in 1950, 14 members out of 50 present had had an unfortunate accident more than once.[2]

Out of 12 general practitioners from whom I received personal communications seven have had that experience at least once. The fallacy in such statistical data is obvious; the data do not reflect the true incidence, as few surgeons care to report.

CONTRIBUTING CONDITIONS AND CAUSES

Of all methods of controlling bleeding during and after tonsillectomy, the use of a loose surgical needle locked in a needle holder is most efficient. It permits better manœuvring in tonsillar fossa and allows for choice of a size of needle suitable to the size of the throat and location of the bleeding vessel. However, the risk of needle breakage or loss should not be underestimated.

The risk of losing the whole needle is increased:

1. When the operator is inexperienced and unskilful.

2. When the emerging tip of the needle, after being pushed through the tissues, is not grasped by a tissue forceps or hæmostat before the needle holder is unlocked. In this risky performance, the surgeon unlocks the needle holder and then grasps with the same needle holder the emerged tip of the needle, which is lying half inserted in the tissues of the fossa. While this is being done, the needle may change its position because of contracture of the tonsil-bed muscles, flow of blood, suction, or change in position of the patient's head. In this situation the needle may become temporarily hidden behind one of the pillars of the soft palate or base of the tongue, or disappear completely.

3. When the number of the catgut used is too small in comparison with the size of the needle eye; the catgut may slip out of the eyelet and the whole needle may get lost.

4. When the shank of the needle rotates in the needle holder; it may unlock the holder and slip out of it (Case 1).

The possible causes of breaking the needle and losing the broken segment are many:[1-3]

1. The needle holder was too heavy, or too much force was applied to the needle.

2. The needle holder and needle were used without previous grasping of the bleeding tissue with a hæmostat.

3. The needle was defective, either poorly manufactured (poorly tempered) or bent by previous misuse.

4. The needle was grasped at its weakest point —at the eyelet.

5. The needle was too thin for the tonsil bed.

6. The patient's head may have moved while the needle was being forced through the tissues of the tonsillar fossa. This movement of the patient's head might be due to inadequate general anæsthesia at the time of suturing, or to clumsy assistance, or to voluntary movement when the

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tonsillectomy was performed under local anæsthesia.

7. The posture of the patient during tonsillectomy has also been blamed for the accident.[4]

8. Elongated styloid process. Fritz[5] reported a case in which the needle, during suture of the left tonsil bed, struck the elongated styloid process and snapped in two. The broken needle, lodged near that process, was recovered six months afterwards.

SITUATION OF SURGICAL NEEDLES LOST DURING TONSILLECTOMY

A suture needle may be lost temporarily and recovered by suction during the course of tonsillectomy, being stuck to the posterior wall of the oropharynx or the base of the tongue (vallecula). It may also become embedded in the tonsillar fossa or the fibres of the superior constrictor pharyngis muscle, or migrate to the parapharyngeal space, into the deep tissues of the neck. It may also become embedded in the muscles of the soft palate bordering the tonsil bed (Case 2). In such instances an additional operation is required for its recovery. The needle has been found as a free foreign body in the nasopharynx,[1, 6] hypopharynx, and pyriform fossa (Case 1). It may pass into the larynx, tracheobronchial tree, œsophagus, or stomach. Weiss[1] advises checking the tubing and suction bottle for the presence of the needle. Cohen[6] in a search for a needle went over the exterior of the patient, the clothing, the anæsthetist, himself, and his assistants and nurses. Nor was the floor of the operating room overlooked. The needle was finally found in the nasopharynx.

In some instances, despite thorough search (personal communication) and repeated operations[2, 4] the needle was never found. It could have been expectorated or swallowed and passed through the natural channels.

COMPLICATIONS

Complications are not uncommon. They occur in 12% of known instances of needle breakage, most of them being serious. Pain in the throat may be vague or follow the pattern of a glossopharyngeal neuralgia. When dysphagia occurs it is very painful. Infections of the parapharyngeal space or lungs are now less frightening because of antibiotics, though one death from pulmonary infection has been reported.[2] Pulmonary infection is a result of prolonged general anæsthesia during an attempt to remove the needle. Fracture of the hyoid bone has occurred during an operation for removal of the broken needle.[1] Migration of the needle into the deep tissues of the neck, as confirmed by roentgenograms, may end in extensive terminal hæmorrhage due to perforation of the carotid arteries by the wandering needle.[4] Swallowing of the needle with perforation of the tracheobronchial tree or œsophagus is another grim possibility.

MANAGEMENT

Our immediate concern after losing or breaking a suture needle is: (1) the general condition of the patient; (2) complete control of hæmorrhage before further search for the needle; (3) immediate lowering of the patient's head to prevent further descent of the needle or its broken fragment.

The step of overwhelming importance is to find the needle. Thorough suction (not sponging) of the nasopharynx, oropharynx and hypopharynx, base of the tongue and its vallecula should be carried out. The tonsil bed where the accident happened should first be inspected by lifting each pillar with an Allis forceps; the tonsil bed and the muscles of the lateral wall of the pharynx are then palpated in search for an embedded needle fragment. The bed of the other tonsil and the soft palate are also palpated. The soft palate is then lifted with Neivert's or Love's retractor and the nasopharynx is inspected under direct vision, the fossa of Rosenmueller, the torus tubarius, the outlets of the Eustachian tubes and the vault serving as landmarks. By pressing the base of the tongue downward and forward the hypopharynx is inspected as much as possible.

If the needle is not seen or felt, direct laryngoscopy with the patient still under anæsthesia may prove of value, as appears from the following personal experience.

CASE 1.—During tonsillectomy on an 8-year-old boy under general anæsthesia, there was profuse bleeding from the left tonsil bed. A curved needle in a holder was inserted in the upper part of the left tonsillar fossa. While the needle was being forced through the tonsil bed, it rotated in the holder, unlocked it and disappeared. In order to remove the needle from the throat, the catgut was pulled on but came out of the patient's mouth without the needle. Immediate suction did not reveal the needle because of the continuous profuse bleeding from the fossa. There was no alternative but to take another needle and suture the bleeding vessel. After control of bleeding and thorough suction, a direct laryngoscopy was performed while the patient was under anæsthesia, and the needle was found in the left pyriform fossa, from which it was safely extracted. Rotation of the needle holder and thin catgut were to blame for the accident.

When direct laryngoscopy does not locate the missing needle, the patient is taken to the x-ray department while under general anæsthesia for fluoroscopy of the neck, tracheobronchial tree, œsophagus and gastro-intestinal tract. The necessary roentgenograms must also be taken. Our procedure now depends upon where the needle or its broken segment has settled.

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A. WHEN THE NEEDLE IS EMBEDDED IN THE TONSILLAR FOSSA

Methods of localization:

A needle embedded in the tonsillar fossa may be easily recognized during fluoroscopy of the neck and on ordinary roentgenograms. The so-called spot x-ray films, though they locate the foreign body, are insufficient in the subsequent attempts to remove the needle. In order to demarcate the position of the needle, Laff[7] inserted an ordinary urethral catheter by way of the nostril into the corresponding tonsillar fossa. The catheter lies along the posterior pillar and in the roentgenograms serves as a marker in relation to the position of the embedded needle.

Davison[8] located an embedded needle by inserting a skin clip in the tonsillar fossa before taking the roentgenograms. Laff[7] discarded this method because of the possibility of having another foreign body besides the one already in existence. Instead he found the combination of a catheter and skin clips very useful. After insertion of the catheter through the nostril, its tip is withdrawn through the mouth and two skin clips are firmly attached to the catheter, one clip to its tip and another one inch above the tip. The catheter with the clips is then returned to the oropharynx so that its tip corresponds to the lower pole of the fossa. Roentgenograms are then taken, which show the position of the embedded needle between the clips in relation to the posterior pillar and upper and lower poles of the tonsillar fossa.

That ordinary roentgenograms without markers may be of little help in recovering an embedded needle is seen from the following experience.

CASE 2.—The patient was a 27-year-old white male referred to our hospital by a general practitioner who had performed a tonsillectomy under ether anæsthesia three days previously. According to the operator, while he was attempting to secure a bleeding vessel low in the inferior part of the right tonsillar fossa, the patient became cyanotic and almost stopped breathing because of some disturbance in the anæsthesia. Being concerned about the patient's condition, the operator lifted his jaw while most of the suture needle was engaged in the tissues of the tonsil bed. At this very moment, the needle broke and disappeared and subsequent suction failed to find it. Upon examination the right tonsil bed appeared lacerated and palpation did not reveal the presence of the needle. Roentgenograms (Fig. 1) taken before our first attempt to recover the broken needle showed a slightly bent needle buried completely under the surface of the right tonsillar fossa, running across the ramus perpendicularis of the mandible. One end of the needle, probably its tip, pointed anteriorly and the other end, probably the broken-off end, was about 1.5 cm. above the angle of the right mandible and somewhat less than 1.5 cm. from the posterior edge of the ramus perpendicularis. After infiltration of the right tonsillar fossa with 1% procaine and upon the operator's insistence that he lost the needle there, a considerable dissection of the lower part of the right fossa was undertaken in a plane at right angles to the position of the needle as indicated in the roentgenograms. Despite dissection for over one hour, the needle was not recovered. The operator's recollection as to the site of the accident was now in doubt, and the need for more accurate localization was apparent. For this purpose two Allis forceps were inserted in the tonsillar fossa, one at its lower end and the other at its upper end, and another series of roentgenograms were taken (Fig. 2). These showed the position of the needle in relation to the forceps. It became apparent that the needle was buried not in the lower part but in the upper part of the fossa, 1 cm. over the tip of the upper forceps, or just over the anterior pillar. These roentgenograms explained why our first attempt to recover the needle was unsuccessful. After additional infiltration of the upper part of the tonsil bed with 1% procaine, blunt dissection 1 cm. over the upper forceps, i.e. over the anterior pillar, located the needle at once in the soft palate muscles bordering the anterior pillar, and it was extracted in a few minutes. It is hard to say whether the operator's recollection of the site of entrance of the needle was misleading or whether it was correct and the needle had migrated during the three days after the tonsillectomy. The utilization of two pairs of Allis forceps as markers was very helpful, while plain roentgenograms were not.

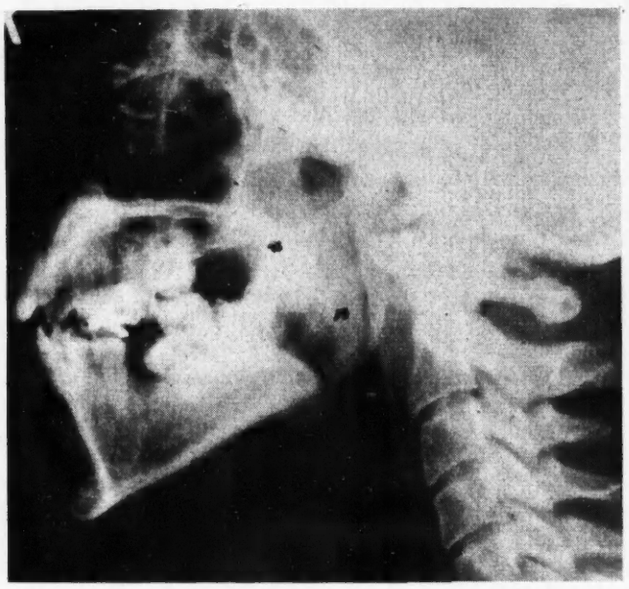

Fig. 1.—Roentgenogram (lateral view of neck) showing broken-off suture needle in region of right tonsillar fossa.

Methods of removal

The following are the methods for removal of a broken suture needle embedded in the tonsillar fossa in order of efficiency:

(a) Attempts to remove an embedded broken segment by dislodging it with a giant magnet or high-powered electromagnet, inserted into the incision wound, have not been successful.[1, 6]

(b) Haphazard dissection supported by digital palpation and ordinary anteroposterior and lateral roentgenograms is not advisable.

(c) So-called blind dissection supported by fluoroscopy, spot roentgenograms and markers is more practical though prolonged and not always effective.

(d) External approach to the parapharyngeal space through an incision in the neck is considered to be practical.

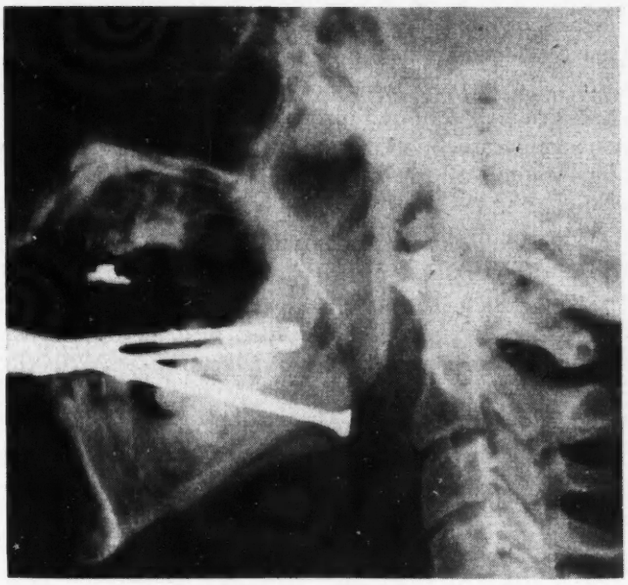

Fig. 2.—Roentgenogram (lateral view of neck) of same patient showing the broken suture needle in relation to the two Allis forceps inserted in the tonsillar fossa as markers.

(e) Amputation of an elongated styloid process may be necessary.[5]

(f) Recovery of the embedded needle with the help of Berman's locator is superior to the methods already mentioned. Even after its location in the tonsil bed by fluoroscopy, spot roentgenograms or markers, the subsequent removal of the foreign body may be very difficult, time-consuming and disappointing because of migration of the needle and tissue distortion. Berman's locator indicates the position of the foreign body while you operate.

The metal locator, devised by Samuel Berman for Moorhead,[9] who used it successfully in removal of an intraspinal bullet at Pearl Harbor, has been employed in removal of broken spinal needles and needles from the heart and knee.[10] Tamari and Bergendahl[4] removed in two instances, with the help of Berman's locator, a broken needle embedded in the tonsillar fossa, within a few minutes. The principle of Berman's locator is that of a mine detector, i.e. of electromagnetic induction. The locator probe in a sterile sleeve is placed in the wound. The locator dial registers the proximity of the needle; while the probe is pressed against each wall of the incision and is raised and lowered, the dial is watched for the highest reading which indicates the depth of the needle and also which wall of the incision contains it. Berman's locator may be used in combination with fluoroscopy and x-ray films. While employing it, all metallic instruments should be removed and wooden tongue depressors and a non-metallic mouth-gag should be used.

(g) Removal under fluoroscopic guidance, as employed and described by Weiss,[1] is very efficient: a Flagg self-illuminating laryngoscope is used for depressing the tongue and for illumination, and an artery forceps is brought into contact with the tonsillar fossa; the laryngoscope is removed and Arens' handscreen type of operating roentgenoscope or a viewing box over the surgeon's eyes is used for fluoroscopic control of the operation. The tip of the artery forceps is manœuvred in the tonsillar fossa until it overlies the embedded needle in the same plane, the tip of the artery forceps is then inserted into the tonsil bed, the jaws are opened and the needle is grasped; the fixed needle is then forced through the tissues until one of its ends appears free in the tonsillar fossa to be seized by another forceps which completes the extraction; or, after the needle has been grasped, dissection under direct vision is performed to expose and remove the needle. Attempts to remove the broken needle without fluoroscopy may take hours; under fluoroscopy it takes minutes to locate the needle accurately.

These are the methods for removal of an embedded needle in the tonsillar fossa. It should be undertaken immediately, though there are reports that it has been done days, weeks, or even months after the accident (the longest interval—18 months[1]).

If the first operation does not recover the needle, it should be located again by any means and ingenuity available.

If attempts to remove the needle have failed, Weiss[1] recommends periodic inspection and palpation of the tonsillar fossa for possible partial extrusion of the needle, and periodic x-ray examination to watch the possible migration of the needle. A needle lodged in the tissues of the tonsil bed or neck, after unsuccessful attempts to remove it, may be symptomless for years (the longest observation periods—four and five years[2, 4]), but is a potential threat to the patient's health.

B. When the Needle is in the Tracheobronchial Tree or Œsophagus

When the surgical needle or its fragment is discovered in the tracheobronchial tree or œsophagus, immediate bronchoscopy or œsophagoscopy is indicated. Simple grasping of the needle with forceps through a bronchoscope or œsophagoscope is dangerous because of possible trauma and perforation of the bronchial or œsophageal wall. In Equen's[11, 12] experience, the needle in such locations can be easily and safely extracted with the help of the Alnico magnet devised by himself in 1945 for removal of ferrous foreign bodies and produced by the General Electric Company. The magnet is 4 cm. in length and 0.3 cm. in diameter and is attached to a urethral catheter for intrabronchial and œsophageal operation. It is small enough to pass through a 4 mm. bronchoscope.

C. When the Needle is Located in the Stomach

The stomach is inflated and a Levin tube used for better manœuvring to approach the needle under fluoroscopic guidance. When the needle has been approached, it is quickly removed by the

Alnico magnet. In Equen's experience[11, 12] the use of this magnet obviated the need for laparotomy, and is superior to waiting and watching for the needle to pass through the intestine with the grim possibility of perforation or obstruction, especially in small children.

PREVENTION

Loss of a suture needle during tonsillectomy may be prevented by employing means of hæmostasis other than a loose suture needle locked in a needle holder. Many surgeons do not use the latter because of the risk involved. The clamp and tie technique as used in the Manhattan Eye, Ear and Throat Hospital will control any tonsillar bleeding, though some operators object to it because of possible recurrence of hæmorrhage due to contraction of the tonsil bed muscle and slipping of the tie.

For beginners who prefer suturing, a one-piece needle and holder is recommended[4] such as the Deschamp needle or any other type of needle whose tip carries an eye with the suture, such as the needles used in vascular and cleft palate surgery (Brophy needle), or tonsil suture needle, right and left (Dupuis-Weiss, Mahoney, Alexander, Walker or Nash needles). If such a needle breaks, the broken fragment can be easily recovered because its tip contains the eye with the tagged catgut. The one-piece needle and holder instrument has the disadvantage of not being readily manœuvrable to meet any demand in controlling the tonsillar bleeding. For this reason the experienced surgeon prefers a loose surgical needle locked in a needle holder, regardless of the risk.

The following precautions may prevent the accident. The needle holder should be light and the needle heavy. Hitschler[2] advocates the use of a suture needle three-fourths of an inch long with a quarter circle curve. The needle should have a strong eye, large enough to be threaded with No. 1 catgut without straining the eye. To prevent rotation of the needle in the holder, Hitschler[2] suggests that the body of the needle should have a square shank and its tip a round shank. Weiss[1] advises testing each needle before using it, discarding thin, bent or damaged needles. Other important preventive measures are featured in the next section.

TECHNIQUE

I shall describe the technique I employ for suturing a tonsillar bleeding point. To locate the bleeding vessel, each pillar is lifted with an Allis forceps. Under continuous suction, the bleeding vessel is found and grasped with an artery forceps with as little neighbouring tissue as possible. The base of the tongue is slid away from the tonsil bed with a Neivert's tongue depressor to make more room for the manœuvring needle. The needle, threaded with No. 1 catgut, is grasped at right angles to the jaws of the needle holder, at least one-third of the length of the needle away from the eye; however, the needle holder should not grasp too much of the curve of the needle. Suturing is accomplished with small circular movements of the needle to avoid excessive pressure on it.

The needle is first inserted beneath the hæmostat in a direction from the posterior to the anterior pillar. When the tip of the needle emerges on the side of the anterior pillar, it is grasped with large tissue forceps and kept there until the needle holder has been unlocked to take over the emerged part of the needle from the tissue forceps and withdraw it from the throat. The still threaded needle is again adjusted at right angles to the jaws of the holder and again inserted, this time above the hæmostat, in the same direction and with the same precautions. The needle is then unthreaded and the suture tied after removal of the hæmostat. Before the catgut over the tie is cut, another check for bleeding is made; if bleeding still persists, a bare needle is threaded with one end of the catgut *in situ* and suturing repeated as outlined above.

MEDICO-LEGAL ASPECTS

Legally, the breaking of a needle during tonsillectomy may be considerd an accident beyond the control of the surgeon, who cannot be blamed for what happens to go wrong. One cannot, therefore, assume negligence merely because the surgeon has lost a surgical needle during the operation. This mishap does not affect his competence or, as Meredith[13] defines it, his standard of proficiency required by law. It is the degree of care the surgeon exercised after the accident that matters. If, according to the evidence, the surgeon failed to describe the accident in the operative records and to notify the hospital authorities, he may be indicted for concealing the mishap and for evading responsibility. Suit for malpractice against him could be brought and a judgment in favour of the patient in the trial court obtained if the surgeon did not try to remove the needle, leaving it *in situ* in the hope that no complications would result. Not telling the patient or his relatives the truth increases the risk of a malpractice action, if complications ensue and the needle is discovered later. In a malpractice suit this would prove that the patient's injury was due to the doctor's failure to employ the required degree of care.

Legal aspects are weighty enough to warrant the removal of the lost needle at the earliest opportunity. According to Meredith,[13] malpractice cannot be established if there is proof of proficiency and proof that the surgeon exercised the required degree of care. The method adopted by the surgeon to recover the needle is scrutinized by independent expert witnesses at the trial. If his method was not in accordance with general and approved practice, judgment may be against him, as illustrated in the following case of breakage of an embedded anæsthesia needle during tonsillectomy, tried in a New York court:[14]

The plaintiff did not blame the defendant, who was an ear, nose and throat specialist, for breaking the needle, but contended that he was negligent in not taking roentgenograms immediately after the accident to locate the needle, trying futilely to remove it by probing the plaintiff's throat and probably pushing the needle further. At the trial the expert witness testified the conduct of the defendant was "a departure from the approved methods in general use", as it was improper to proceed with the tonsillectomy after the accident since a broken needle is immediately sucked into the muscles, and that the defendant did not exercise a great degree of skill trying to remove the needle without roentgenograms by probing instead of recovering the needle by an external approach to the parapharyngeal space. The plaintiff obtained a judgment in his favour.

According to Meredith,[13] the question of what was "approved practice at the time" is of great importance in any malpractice suit, and means "a practice approved by at least a respectable minority of competent practitioners in the same field".

SUMMARY AND CONCLUSIONS

Losing a surgical needle during a tonsillectomy is a complication more challenging than the bleeding itself. Uncertainty is the main feature of this complication, matched by its seriousness. Often an apparently easy case becomes exasperating and frustrating. The lost needle may be found quite distant from the tonsillar fossa. Before one attempts to remove the needle, it should be accurately located. Accurate location may be difficult, and also subsequent removal, but the more time is spent in locating the needle, the less time will be required to remove it. The foregoing outline of contributing conditions and causes, and principles of management and prevention, may be helpful in coping with this accident.

The lost needle should be recovered at the earliest opportunity. It is stressed that a retained needle is a potential source of serious complications, is a source of anxiety to patient and surgeon, and may involve the surgeon in a malpractice suit. The success of his defence would depend upon his standards of proficiency, conduct and care exercised after the accident.

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5 Dunlop Block.

RÉSUMÉ

La perte d'une aiguille au cours d'une amygdalectomie est une complication encore plus difficile à enrayer que l'hémorragie même. L'incertitude qu'elle engendre n'a d'égal que la gravité de la situation. Un cas qui s'annonçait simple peut par le fait même devenir exaspérant et décourageant. L'aiguille perdue se loge quelquefois assez loin de la fosse amygdalienne. Il convient donc avant d'en entreprendre la recherche d'en faire la localisation précise, ce qui peut être aussi difficile que sa récupération. Meilleure la localisation, moins ardue sera l'extraction de l'aiguille perdue. L'auteur offre des conseils utiles sur la prévention de tels accidents et la conduite à tenir dans ces cas. Comme cette aiguille peut devenir la source de complications très graves, il importe de la retrouver au plus tôt: une fois extraite, le chirurgien et son malade ne s'en porteront que mieux. Si l'opérateur devenait impliqué dans une poursuite légale à ce sujet, le succès de sa défense dépendrait du degré de compétence dont il fait part dans sa pratique quotidienne, de la conduite qu'il a tenue après cet accident et du soin qu'il a apporté à le réparer.

Case Reports

VISCERAL LARVA MIGRANS

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AMONG ALL the cases of profound eosinophilia, visceral larva migrans has received considerable interest and attention in the last ten years. This is essentially a disease of toddlers who have close association with dogs and cats, and a habit of eating dirt. In addition to eosinophilia and hyperleukocytosis they show hyperglobulinæmia, hepatomegaly and episodes of fever.

Before 1947, many of these cases were described under various titles. In 1947, Perlingiero and György[1] reported the clinical course of a two-year-old Negro child who presented many features of the syndrome. In their case, an adult ascarid was vomited. They related the clinical findings as well as the hepatic lesions to an allergic response to the ascaris toxin.

In 1949, Zuelzer and Apt[2] comprehensively studied eight cases, with autopsy findings in one. They grouped these cases into a syndrome of distinct clinical unity. The etiology was not known but the condition was assumed to represent the allergic response to some unknown antigens.

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Mercer *et al.*[3] in 1950 were able to demonstrate an etiologic agent, the larval ascaris, in a liver section taken by biopsy from a child who had all the typical manifestations of the syndrome. Allergy to ascaris was again thought to play an important part in the production of this clinical entity. In their case, improvement was obtained after the administration of antihistamine but hexylresorcinol therapy did not seem to alter the course.

In 1951, Behrer[4] described another case with all the cardinal features. For the second time larval ascaris was found in the liver section obtained by biopsy.

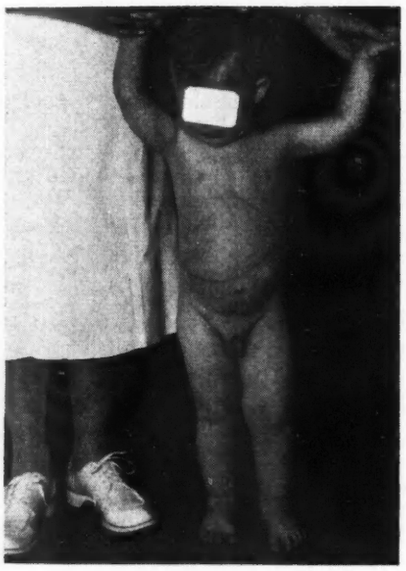

Fig. 1

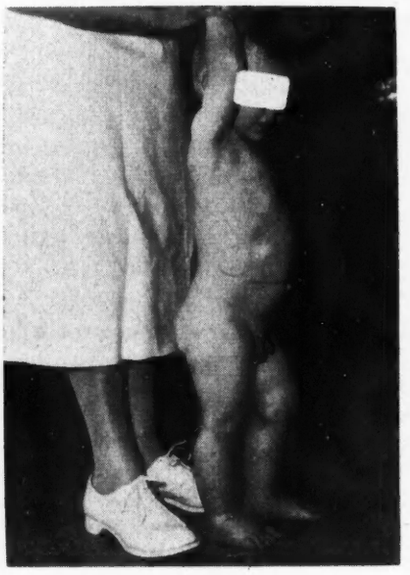

Fig. 2

In 1952, Beaver and his collaborators[5] studied three cases of chronic eosinophilia with granulomatous lesions in the liver. A larval nematode observed in sections from the liver of one patient was identified either as *Toxocara canis* or *Toxocara cati*. They also suggested that the larval nematode described by Mercer *et al.* and Behrer was more likely to be Toxocara than human ascaris. The term "visceral larva migrans" was introduced by them for this type of parasitism. Silver *et al.*[6] in the same year reported a 27-month-old child with all the clinical manifestations of the syndrome. They demonstrated an elevation of heterophil antibodies of the serum sickness variety.

The second known death apparently due to this disease was reported by Brill[7] in 1953. Granulomatous lesions of specific structure were found in the heart, liver, kidneys and lungs. A Toxocara larva was demonstrated in one of the pulmonary nodules. In the same year Milburn and Ernst[8] presented an analysis of 15 reported cases including one of theirs. Eleven cases had liver biopsy which showed the characteristic eosinophilic infiltrations and granulomatous lesions. At that time, Dent and Carrera[9] also studied seven cases with very similar clinical pictures. Smith and Beaver[10] proved experimentally that the infective stage of the larval nematodes persisted for a considerable period of time. They produced this clinical syndrome by feeding embryonated eggs of dog ascarids to experimental animals and humans.

To our knowledge, Fellers in 1953[11] was the first to make agglutination studies on a child with this syndrome. The antigen he used was prepared from freshly obtained roundworms, the human and dog ascarids. The test was considered to be diagnostic.

In 1956, Heiner and Kevy[12] described three siblings with this disease in varying degrees of severity. An urticarial eruption was described in one patient. They emphasized the finding of unusually large vacuolated eosinophils. A serological test using the precipitin reaction against toxocara antigen was found helpful in the diagnosis. Karpinski[13] reported two additional cases showing larva of *Toxocara canis* in a liver biopsy. They proposed the term "larval granulomatosis" for this condition. The potential hazard of household dogs and cats was emphasized as a public health problem.

It is the purpose of this paper to report the case of an 18-month-old infant who presented all the cardinal features of this syndrome.

An 18-month-old infant was admitted to Regina Grey Nuns' Hospital on May 18, 1957, with a tentative diagnosis of acute leukæmia.

Nineteen days before admission, the baby was thought to have a cold. The following day he began to cough and this persisted for a week. Four days later, he started to run a remittent type of fever. His temperature rose as high as 105° F. in the afternoons and evenings. His appetite was greatly impaired. He became very listless and irritable. "He whines all day." He was examined by his family physician during the second week of his illness and nothing abnormal was found. He was admitted to the local hospital, where

TABLE I.—LABORATORY FINDINGS—C.B., AGED 18 MONTHS

Date	Hb. (g.%)	Total W.B.C. (per c.mm.)	Eosinophils %	Sed. rate (mm./hr.)	Total serum protein (g.%)	Alb./glob. ratio	Thymol turb. (units)	Cephalin flocculation 24 hours	Cephalin flocculation 48 hours
May 18	8.8	74,500	51	42.0					
May 22	8.2	65,500	68		6.6	3.8/2.8	14.75	3 plus	4 plus
May 28	10.8	43,900	81		7.2	3.7/3.5		3 plus	4 plus
June 3	10.9	23,300	63						
June 7	11.6	16,600	60		7.3	4.3/3.0	13.5	2 plus	2 plus
June 12	11.5	17,200	50	36.0					
June 17	11.7	27,000	56						
June 24	12.4	31,000	60	46.0	7.0		14.25		
June 30	11.3	15,900	19	40.5	7.0	4.2/2.8	12.7	trace	2 plus
Dec. 10	12.7	10,700	18				4.9	sl. trace	sl. trace

peripheral blood examinations were made and leukæmia was suggested. Two days later, he was referred to one of us (O.E.L.) for further investigation. No evidence of purpura or jaundice had been noted.

His only past illness was a mild eczema of the face when he was three months old. He practically lived on a milk diet, as he refused all solid food. No vitamins had been given. He and his family lived on a farm and drank unpasteurized milk.

The family history revealed that his maternal grandmother, several aunts and his sister had had hay fever and eczema.

Physical examination on admission revealed a well developed and fairly well nourished child who was extremely irritable. Pallor was quite marked but there was no jaundice or petechiæ. His temperature was 104° F. There were no enlarged lymph nodes. The chest was clear. The abdomen was enlarged but there was no demonstrable ascites. The liver was huge, with its edge extending six cm. below the costal margin. Its surface was smooth, firm and not tender. The tip of the spleen was just palpable. There was obvious puffiness of the legs, especially the dorsum of the feet. The œdema did not pit on pressure (Figs. 1 and 2).

Laboratory investigation showed anæmia, hyperleukocytosis with profound eosinophilia (Table I). The platelet count was normal. Bone-marrow study showed an increased percentage of eosinophils but there was no evidence of leukæmia. Abnormal eosinophils were seen in the peripheral blood. Many of them were bilobed and large, with vacuolated cytoplasm (Fig. 3). Repeated blood cultures were sterile. Agglutinations against typhoid, paratyphoid and brucella were negative. Repeated stool examinations failed to reveal any parasites or ova. Tuberculin tests were negative. Serum iron was 20 μg. %.

Roentgenograms of the chest and long bones showed no abnormalities.

In view of the profound eosinophilia, the possibility of larval infection was considered. On further questioning of the mother, the following pertinent information was obtained. The baby had a habit of pica and his mother caught him on numerous occasions eating dirt. The family puppy and kitten were great companions of the baby. "They are together all day long." His mother even recalled having seen him eating something like the excreta of the kitten. She had never noticed that the puppy, kitten or the baby passed a worm.

Further investigation showed abnormal liver function tests. Total serum protein ranged from 6.6 to 7.3 g. %, with the globulin level ranging from 2.8 to 3.5 g. %. Electrophoresis showed slight elevation of gamma globulin. Heterophil antibody agglutination was negative. Skin test for trichinosis was negative. Skin test using the antigen of *Toxocara canis* (courtesy of Dr. R. C. Jung of Tulane University) was strongly positive while two controls were negative. His serum was sent to Dr. Jung for hæmagglutination. The titre was 1 in 1280 with Ascaris antigen and 640 with Toxocara antigen. These findings were considered definitely significant for infection with Toxocara or a worm antigenically closely related.

A week after the child's admission, the family cat was reported to be sick. At the mother's request an autopsy was done by Dr. Abelseth, veterinarian of the Saskatchewan Provincial Laboratory. Two dozen adult roundworms found in the duodenum were identified as *Toxocara canis* or *cati*. Examination of the yard dirt and stools from the dog and the cat failed to reveal any parasites or ova.

The remainder of the family were tested and showed no eosinophilia.

For the first week in hospital, the baby continued to run a remittent high fever. On the fifth hospital day while his temperature was again 104° F., he suddenly went into a shocked condition with marked cyanosis of lips, hands and feet. The skin was mottled and icy cold. He was given Chlortripolon (chlorpheniramine) 4 mg. intramuscularly. Gradually his skin colour returned. He was kept on Chlortripolon for five days. The temperature then started to taper off and he

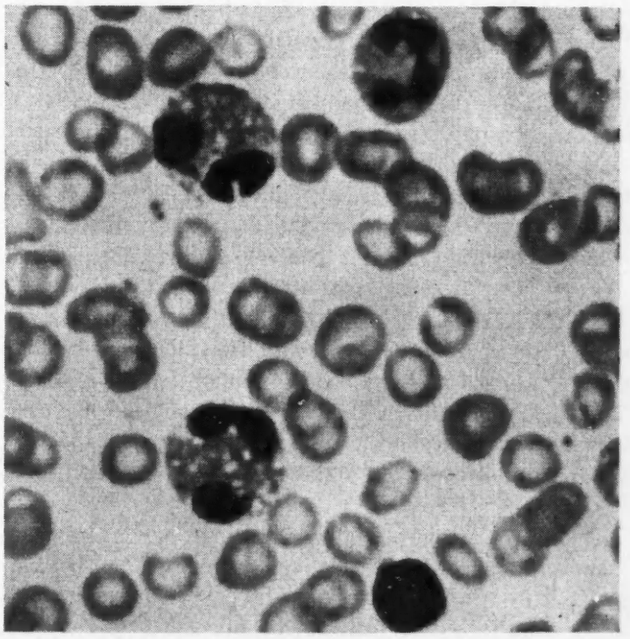

Fig. 3

became afebrile for two weeks. His appetite and disposition improved. However, a moderate fluctuating fever recurred on June 15, 1957, and lasted for nine days. He was transfused on two occasions because of anæmia. A high protein, high caloric diet with extra vitamins was given. The size of the liver decreased considerably, although it was still two cm. below the costal margin on discharge. The œdema of legs disappeared. He was discharged on June 26, 1957, afebrile and happy.

Since discharge, he has had two bouts of moderate fever each lasting for three to four days. He is eating well and his disposition is greatly improved. However, he still has the habit of pica. He was seen on July 30, 1957, and again on December 10, 1957. His colour was excellent. His liver was no longer enlarged. Liver function tests had returned to normal and eosinophilia had dropped to 18%.

DISCUSSION

This syndrome probably occurs more often than the number of reported cases indicates.[12, 14] As is true of many diseases, the diagnosis is easily made when it is thought of. The case reported here presented itself in a rather typical fashion. The classical patient is a pale or irritable toddler who plays intimately with a puppy or kitten and has a habit of eating dirt. The majority of reported cases are in children between 18 months and three years of age. The history of pica and a close relation with pet dogs and cats may not be obtained when the patient is first seen.

Many of the reported cases are referred to hospital for investigation of leukocytosis with eosinophilia. The condition may be missed if only the total white cell count is done, as it may be normal or only slightly elevated. In the majority of cases, the total white cell count is greatly elevated. It has been reported as high as 100,000 per c.mm. Eosinophilia is invariably marked and has been reported as high as 80%. In our patient, the total white count varied from 16,000 to 74,500, with eosinophils ranging from 50% to 80%. In the literature, unusually large eosinophils with vacuolated cytoplasm were found in some of the cases.[12] These abnormal cells were predominant in the peripheral blood smear of our case.

The history of allergy in many of these cases is of interest. Many of them have a family history of allergy, or the patient himself has some form of allergy. Our patient is another example of this.

Hepatomegaly is a usual finding. In asymptomatic cases, the liver may not be enlarged. In our patient, hepatomegaly was a conspicuous feature. The size of the liver decreased as the temperature declined. Even when he was afebrile, hepatomegaly was pronounced. Splenomegaly is not a common finding.

Hyperglobulinæmia (especially hypergammaglobulinæmia) is almost a constant finding. It was present in 10 of 11 cases in which fractional protein determinations were made. In our case, the serum globulin level ranged from 2.8 to 3.5 g. %. Serum electrophoresis showed an increase of gamma globulin.

An interesting finding which has not been reported previously was œdema of the legs. Œdema of the lips was described in one of the earlier reports.[1] Leg œdema in our patient was very similar to that seen in angioneurotic œdema. It disappeared gradually as the temperature became normal.

Until recently, all the cases were diagnosed solely by liver biopsy, which showed extensive granulomatous lesions. Larval nematodes have been observed in the liver sections. Marked infiltration by eosinophils is always conspicuous.

The diagnosis of this syndrome can be made with considerable certainty on clinical grounds alone, as routine liver biopsy is now considered unnecessary. Abnormal eosinophils should be looked for. Recently both Jung[13] and Heiner[12] have made encouraging progress towards the development of serological aids in the diagnosis of this syndrome. We obtained some antigen for *Toxocara canis* from Dr. Jung. The skin test was strongly positive in our patient while two controls gave a negative result. However, the skin test is hardly conclusive as it is somewhat non-specific. The finding of high hæmagglutination titres with Ascaris antigen and Toxocara antigen is more diagnostic.

The differential diagnosis includes acute eosinophilic leukæmia, familial eosinophilia, *Capillaria hepatica* infection, eosinophilia due to other allergic diseases, and polyarteritis nodosa. Eosinophilic leukæmia is extremely rare. A complete hæmatologic study including bone marrow aspiration should suffice to distinguish it from the benign syndrome of visceral larva migrans. In the latter condition the characteristic invasion of the marrow by blast forms is not seen. However, differentiation from early leukæmia may require several marrow examinations.

The so-called "familial eosinophilia" had been reported in families whose members exhibit a chronic eosinophilia. This is a poorly defined entity, and many cases of eosinophilia described in the literature as "hereditary" or "familial" may in fact represent systemic involvement by the larval forms of Toxocara, Ascaris or hookworm.

Eosinophilia due to systemic invasion by other parasites may present the most difficult problems of differential diagnosis. The larvæ of *Ascaris lumbricoides* (human roundworm) may on rare occasions produce a syndrome identical to visceral larva migrans (see Fig. 4). Skin testing and the previously described complement fixation tests may be helpful in diagnosis. The finding of Ascaris or their ova in the stools is evidence in favour of this entity. However, Ascaris has been found to co-exist in definite Toxocara infections. Löffler's syndrome should be considered whenever moderate or marked eosinophilia is found. In this condition wheezing and pulmonary infiltrations are the predominant features. This syndrome is found more commonly

in older children and adults, while visceral larva migrans is chiefly a disease of infants.

"Creeping eruption" or cutaneous larva migrans represents an interesting parallel to visceral larval migrans in that the causative agent, *Ankylostoma braziliense*, only develops to the adult stage in dogs and cats (see Fig. 4).

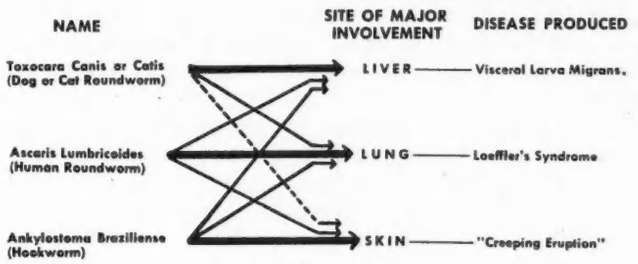

Fig. 4

Febrile episodes and eosinophilia may bring up the possibility of trichinosis. Skin testing, complement fixation reactions and, when required, muscle biopsy may be necessary to differentiate it from systemic Toxocara infections.

A recently described and exceedingly rare infection with *Capillaria hepatica* may produce a syndrome identical to visceral larva migrans. Capillaria is a nematode of the Trichuris family. It commonly infects the liver of the rat, and human infection occurs only through the ingestion of fæcal matter from an animal that has ingested infected rat liver. Liver biopsy is the only means of differentiating this disease from visceral larva migrans.

Serum sickness and polyarteritis nodosa display certain manifestations in common with visceral larva migrans. However, splenomegaly, lymphadenopathy and joint effusions are rare manifestations of visceral larva migrans but are seen commonly in serum sickness. Neither serum sickness nor polyarteritis shows the striking eosinophilia or hepatomegaly seen in Toxocara larva invasions. The abdominal pain, hypertension, cardiac and renal involvement seen in polyarteritis are not features of visceral larva migrans.

The prognosis of this syndrome is generally favourable. In asymptomatic cases, the child may be normal in every respect except for the persistent eosinophilia, which may last for many months to over a year. In moderately severe cases, the child may run an intermittent fever, and have an enlarged liver or repeated bouts of wheezing for several months. The patient in fulminating cases may be extremely ill with severe respiratory distress. Three deaths have been reported.

Treatment is simply supportive. No drug therapy has been found to alter the course. The source of infection such as infected household pets should be eliminated. An attempt should be made to control the habit of pica. Where toxicity due to the disease is overwhelming, cortisone and ACTH probably should be used, but their value has yet to be conclusively proven. There may also be times when antihistamines are of value. Our case may have derived some benefit from the use of parenteral Chlortripolon.

SUMMARY

Visceral larva migrans is a recently recognized clinical syndrome. It is characterized by persistent marked eosinophilia, leukocytosis, hyperglobulinæmia and hepatomegaly in an infant or young child who has close contact with household pets and a habit of eating dirt.

The diagnosis of the syndrome can be made with considerable certainty on clinical grounds alone. The prognosis of the syndrome is favourable.

An additional case of an 18-month-old infant with this syndrome is presented.

We wish to acknowledge the kind assistance of Dr. M. K. Abelseth of Saskatchewan Provincial Laboratory for the identification of Toxocara in the offending cat. We are very grateful to Dr. R. C. Jung of Tulane University for his advice and serologic studies.

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VAGINAL OCCLUSION AND CRYTOMENORRHŒA

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THE CLASSICAL DESCRIPTION and illustrations of imperforate hymen and its sequelæ in the menstruating adolescent are presented in all textbooks of gynæcology. The anomaly is a condition to be kept in mind by practitioners rather than an entity likely to be encountered. The following case report presents a variation of the condition which led to a completely wrong diagnosis.

J.N., aged 19, was brought to me by her mother on May 12, 1954, for investigation of secondary amenorrhœa which had been present since July 1952. The menarche was in July 1951 at the age of 16. The periods had occurred at intervals of four to six weeks, with moderate dark brown flow lasting for five or six days. There was no history of dysmenorrhœa,

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and no volunteered complaint of pain since the onset of the amenorrhœa.

The girl was well built and had marked adolescent acne and a tendency to hirsutism. Palpation of the abdomen revealed a mobile, spherical mass, 12 cm. in diameter, lying 4 cm. below the umbilicus and to the left of the midline. The mass was definitely cystic and not tender. Its mobility was such that close questioning was done to elicit any history of pain which would suggest possible episodes of partial torsion. The girl said that she did have occasional abdominal cramps but was not specific as to their severity or periodicity.

The external genitalia were normal. The vaginal introitus was patent with an opening sufficient to admit the tip of the little finger; an intact crescentic hymen was present. The girl was very resistant to examination of the genitals, and rectal examination was done with great difficulty. The cul de sac was occupied by a boggy tumour which was thought to be the lower pole of the abdominal mass; no other pelvic structures could be made out.

The amenorrhœa, acne and hirsutism suggested a diagnosis of arrhenoblastoma. Other ovarian neoplasms or a bizarre mesenteric cyst were also considered possibilities. The mobility of the tumour made torsion a distinct hazard and therefore early laparotomy was advised. A Friedman test done as a matter of interest was negative.

Laparotomy was undertaken on May 26. On opening the abdomen a pinkish mass appeared to occupy the whole pelvic basin. Displacement of the intestines upwards brought the complete picture into view. The mass, so mobile on palpation through the abdominal wall, was the uterus, distended to 10 cm. in diameter, and perched obliquely on the upper end of the vagina which was distended to a diameter of 16 cm. A fluid wave passed readily from the fundus to the lowest part of the vagina. The uterus was flanked by sealed and distended Fallopian tubes which contained fairly firm masses in the distal portions. Both ovaries were normal, the left containing a corpus luteum. The diagnosis was obvious: hæmatocolpos, hæmatometra, and hæmatosalpinges in a girl who had had apparently normal menstrual periods for a year, and who did not have an imperforate hymen.

The anæsthetist remarked that the patient's blood pressure was remaining constant at 140/90 mm. Hg, which was unusually high for a girl of nineteen. He suggested the possibility of an adrenal tumour. Palpation of the adrenal glands showed the right one to be somewhat larger than the left, a finding which may be of diagnostic help in future should the girl continue to show an elevation of blood pressure.

The appendix was removed and the abdomen closed.

The patient was redraped in the lithotomy position for vaginal investigation. The normalcy of the external genitalia was confirmed, but on breaking the hymen and pushing the finger into the vaginal canal an obstruction was met about 3 cm. from the introitus. A midline episiotomy was done to give exposure and a transverse septum was revealed, ragged in appearance and with a dimple at its centre. The dimple was probed firmly with eventual break-through of the uterine sound to a distance of 2 cm. where another obstruction was encountered. The opening in the first septum was enlarged to permit insertion of a finger and the second cavity was explored. No menstrual debris was evident as yet. The second septum had a depression against the right vaginal wall; this was broken down by the probing finger, resulting in a trickle of dark brown fluid. Both openings were spread to admit two fingers and an immediate gush of thick brown-black fluid occurred. The fluid continued to drain away in a steady stream for ten minutes; with each respiration a temporary increase in rate of flow occurred. It was estimated that at least 40 ounces of encysted menstrual fluid was evacuated.

Palpation then revealed the cervix hanging loose and dilated, as in the immediate postpartum state. Swabbing of the vagina showed that the area bounded by the two septa was rough and poorly epithelialized. In order to prevent the raw surfaces from adhering and yet not to interfere with drainage from the upper regions of the distended organs, a gauze wick soaked in liquid petrolatum and impregnated with sulfathiazole powder was inserted up to the uterine cavity. The episiotomy was repaired transversely.

The gauze wick was removed in 48 hours with some difficulty because of the vigorous protests of the patient. As it was essential that the vagina be kept open and the co-operation of the girl could not be gained, it was necessary to anæsthetize her to inspect progress and to reinsert a wick. This was done on three different occasions during the next two weeks. The patient was put on large doses of œstrogens to help speed epithelialization of the raw vaginal walls. Her postoperative course was quite satisfactory and she was discharged three weeks after admission, at which time the vaginal canal admitted two fingers easily throughout its length and the cervix was 4 cm. in diameter.

Close questioning of the girl and her mother elicited no history of trauma which might have injured the vagina. It is possible that a degree of vaginal occlusion was present as a congenital anomaly, allowing partial escape of the menstrual debris during the year in which the girl was having periods, and that retention of some menstrual elements resulted in irritation and excoriation of the proximal vaginal mucosa causing adhesive total occlusion.

Examination one month after discharge from hospital showed the vaginal walls tending to contract although the canal admitted one finger readily throughout its length. The cervix was 2.5 cm. in diameter with a wide os. There was marked improvement of the epithelialization of the vaginal mucosa, and also incidentally of the acne. Nothing resembling a menstrual period had occurred.

Œstrogenic therapy was continued in the form of a vaginal cream, the applicator being useful as a means of insuring that the vagina would remain patent. A menstrual period occurred eleven weeks after operation, the œstrogenic therapy having been discontinued a few days previously.

The young woman has been examined at intervals during the past three years. The menstrual cycle is completely regular and normal. The

vaginal canal admits one finger throughout its length and the walls are less resistant than formerly. The cervix and uterus are normal and no adnexal masses are palpable. Her blood pressure remains at a high level for her age but has not risen above 140/90 mm. Hg. No masses are palpable in the upper abdomen. She will continue to report for periodic examinations.

SUMMARY

A case is reported of a 19-year-old girl who had hæmatocolpos, hæmatometra and hæmatosalpinges due to an occlusion in the upper part of the vagina. She had an apparent normal menarche at the age of 16, with secondary amenorrhœa developing one year later. An incidental finding was a slightly enlarged right adrenal with persistent elevation of blood pressure.

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ENDOMETRIOSIS OF THE COLON AND FIBROIDS

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OCCASIONAL bowel motions in the form of "goat's droppings", together with increasingly heavy menstrual periods sufficient to cause constitutional sequelæ, were the cause of this patient's being referred for gynæcological opinion at the age of 45; she had had a gynæcological operation when she was 34 years of age.

The patient had been married at the age of 19. Her first baby was born the following year and the second three years later, the pregnancies being spaced by the avoidance of coitus for the first 18 days of the menstrual cycle; three years later she had a spontaneous abortion and thereafter there were no further pregnancies, despite attempts to conceive. This caused her to seek gynæcological advice in 1944, when she was 34 years of age, resulting in the performance of a myomectomy and Gilliam suspension. The next pregnancy occurred three years later, when she was 37, and was complicated by antepartum hæmorrhage from the 34th week of gestation, for which no cause was found: her fourth and last pregnancy occurred the following year and resulted in the normal delivery of a live baby after which she reverted to her former employment of the "safe period".

In May 1955, she was referred to me because her periods had become more frequent and heavier over the preceding five months. The loss was now such that she had to lie down for the second day of the flow, because the severity of the bleeding made her feel weak. Since her last confinement the menstrual loss had been noticeably heavier and especially so in the last three years, necessitating the use of 12 "large" sanitary pads daily. There was a large amount of blood clot, especially obvious after lying down.

She also complained of pain, coming on about a week before the period, and chiefly noticed when turning on to her left side while lying down. There had been some dysmenorrhœa from her menarche at the age of 16; the dysmenorrhœa had persisted despite the three pregnancies, and interfered with her carrying out her household duties until the performance of the Gilliam suspension. There was no similarity between the pain of which she now complained and the intramenstrual pain.

She had a regular daily bowel action; when she neglected the call the motion would be prolonged and the fæces would take on the form of "goat's droppings". Occasionally during the menses there was suprapubic pressure pain.

She was a well-nourished woman of somewhat sallow complexion, rather overweight but otherwise normal and healthy. No masses were felt on abdominal palpation and no tender areas were discovered.

Vaginal examination disclosed a deficient perineum, urethral descent, slight cystocele and a minor degree of rectocele; the cervix was bulky and eroded, the uterus in anteversion, firm in consistency but irregularly enlarged to about the size of an eight-weeks' pregnancy.

She was thought to have developed further fibroids with possible adhesions to the old myomectomy scar, and abdominal total hysterectomy was advised and agreed upon.

The abdomen was opened through the old scar. Ileum was adherent to the peritoneal surface; there were many adhesions of the small bowel, the bladder being adherent to the anterior fundus of the uterus, which was the site of numerous small interstitial fibroids; the pouch of Douglas was completely obliterated by adhesions, and the right ovary was attached by a thick band to the posterior parametrium, on its own side of the pelvis. At the level of the recto-sigmoid junction there was a hard circular stricture of the bowel about ¾ to 1 inch in depth and apparently encircling the lumen (with no disruption of the serous covering). Despite the pelvic adhesions this mass appeared to be comparatively free and mobile, well above the examining finger on routine rectal examination. As there was a strong possibility that the stricture was malignant and that abdomino-perineal resection would be necessary, it was decided to restrict operation to bilateral oophorectomy at that juncture, and to resect the diseased portion of bowel later. Accordingly both ovaries were removed and the abdomen was closed.

Sigmoidoscopy revealed a firm and undilatable stricture of the lumen of the bowel about 6 inches proximal to the anus, the aperture being about ⅜ inch in diameter; the mucosa overlying the stricture appeared healthy but it was not possible to pass the instrument above its lower margin. A portion of the distal mucosa was removed for microscopy; the report on this was negative. The ovaries were reported as containing corpora lutea and otherwise nothing of note, though at operation plaques were noted on the surface of the right ovary suggestive of endometriosis and also an area suspicious of aberrant endometrium on the posterior surface of the uterus.

It was decided, in consultation with Mr. C. L. McDowell who had seen the pelvis at the time of lapar-

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otomy, that as the possibility of malignancy had not been ruled out it was best to resect the suspected portion of bowel after preliminary curettage to remove any possible intrauterine polypi. This was accordingly carried out under an "antibiotic umbrella" of chloramphenicol on the 7th day after the first operation. An anterior resection of the colon was satisfactorily performed, a transverse colostomy done at the same time, a glove drain inserted to the site of anastomosis for 48 hours and the abdomen closed; two pints of whole blood were transfused.

Convalescence was entirely normal, the colostomy being closed on the 15th postoperative day; the bowels moved normally from the 8th day after this closure, the patient being discharged home on the 20th day after oophorectomy.

When she was seen again a fortnight later, the wounds were well healed and her general condition was satisfactory. There was slight tenderness on rectal palpation of the anastomosis, and the bowel action had not completely returned to routine. The uterus appeared to be somewhat smaller than at operation and was in good position, there had been no further uterine bleeding and the patient felt greatly improved in that short time.

Pathological Report (Dr. Joan McCarthy, Trinity College, Dublin).

Ovaries—Macroscopically: The larger ovary, soft and cystic; the smaller slightly cystic and contains two corpora lutea. Microscopically: Nothing of note in the ovaries.

Colon—Biopsy specimen: Sections show normal mucosa.

Sigmoid—Macroscopically: Small hard, fibrous mass present in colon, extending for about 3″ around the bowel wall. Microscopically: Sections show endometriosis of the wall of the colon; some of the glands lie deeply in the muscle coats. There is no evidence of malignancy.

Endometrium—The curettings are very much fragmented but such glands as are present appear to be hyperplastic. There is no evidence of malignancy.

DISCUSSION

Endometriosis is a common condition and the aberrant tissue may be found in a number of sites, among which the utero-sacral ligaments, the peritoneum of the pouch of Douglas and the pelvic colon rank high in order of frequency; however, the implants (if this be the method of spread, as I believe) are usually to be found on the surface of the host organ and not in the wall, as in this case; moreover, the symptoms produced can usually be explained by an increase in pressure in the enclosed endometrial glands rather than a non-cyclic interference with the normal action of the organ the main symptom of course being a distinctive type of pain associated rather with the postmenstrual phase than at the time of the menses themselves. I have recently heard of a case where endometriosis of the terminal ileum gave rise to small bowel obstruction at the menses.

The course adopted in dealing with this case is open to a considerable degree of criticism. Had a stricture been diagnosed before the primary operation, it would have been best to combine the resection of colon with a total hysterectomy. This would have given the optimum outlook for this patient, for she is still in possession of an organ enlarged by tumour growths (admittedly innocent and likely to undergo atrophy) and has a cervix which though not malignant is, to say the least, unhealthy. The removal of her ovaries was inevitable, and the risk of a severe artificial menopause and future mental changes is one that had to be taken.

Would the stricture of the colon have resolved as a result of the oophorectomy? and was the resection therefore unnecessary? At the time of inspection of the bowel from outside and inside the lumen, we considered that she was in danger of a possible acute obstruction if at any time she ingested any solid object larger than a cherry stone.

The resolution of the parasitic tissue might well be expected to cause a fibrous stricture of the bowel when the scar tissue replaced it, and she could then look forward to possible chronic and maybe progressive obstruction with subsequent acute obstruction. Since this case, however, I have been told of a similar case of stricture of the large bowel where conservative measures were taken as regards the colon; after a panhysterectomy (both ovaries and cervix removed) there was no sign of the stricture on sigmoidoscopic examination two months after operation.

Finally, and most important, the true nature of the stricture was not satisfactorily established until the specimen was examined pathologically. However, the patient's condition was so good at the close of the second operation that one is left with a sense of regret that hysterectomy was not then carried out.

SUMMARY

A case of circular endometriosis of the colon with alteration of bowel motions but no other signs or symptoms and little cyclical alteration of defæcation, presenting with uterine fibroids, is described; the treatment is criticized and evaluated.

PSYCHIATRY AND CRIMINAL LAW

"There is no responsible thinker or writer on the criminal law who fails to perceive the great degree to which criminals are conditioned by the circumstances of their environment and of their birth and genetic inheritance. Perhaps the truth of the matter is that whether one accepts or rejects a primarily determinist philosophy, it is necessary to hold people imputable for their crimes, punishable for their crimes, unless it can be established that they clearly were not so. Our techniques of social control may thus have to be relatively blunt and unsophisticated instruments. What does, however, seem a considerable pity is that the social sciences, which are gradually building up some deeper understanding of man and his environment, do not yet seem to have had a profound effect upon the shape, content and operation of our criminal law."—Norval Morris, Beattie-Smith Lectures, Part I, *M. J. Australia*, 1: 313, 1958.

EXTRAVASATION OF URINE SECONDARY TO URETERAL CALCULUS, WITH STUDY 21 YEARS LATER

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EXTRAVASATION of urine secondary to ureteral calculus is an unusual occurrence. When it happens, however, the events are usually dramatic. Several of the more recent books on urology make no mention of this complication, though many of these discuss in detail surgical and traumatic accidents to the ureter. Winsbury-White[1] discussed the condition briefly in his textbook. Some factors in the case being presented are at variance with other reported cases. There was an opportunity to study the kidney and ureter 21 years after the initial illness.

H.C, a married woman, aged 20, was seen in consultation on January 28, 1936. The patient had had an uncomplicated confinement a few weeks previously. She was admitted to hospital with severe right-sided pain. She had a temperature of 105° F. and there was a tender mass filling the right loin. A radiograph showed a shadow in the region of the right kidney and another in the region of the lower right ureter. A diagnosis of perinephritic abscess was made. On the way to the operating room an intravenous pyelogram was done (these films are no longer available). The radiologist's report read: "Diodrast shows the left kidney appearing normal and apparently has normal function. The pelvis and calices of the right kidney are greatly dilated and there is a definite stone in the upper calyx; the lower part of the ureter is not visualized but the dye apparently leaks out of the ureter into the surrounding tissue at the level of the fourth lumbar vertebra; the possibility of a ruptured ureter forming a perinephritic abscess is suggestive."

Through a right loin incision the abscess was drained; a large quantity of bloodstained fluid with a little thin pus was liberated. The kidney was not explored; drainage was provided. Two weeks later the stone was removed from the lower ureter. There was prompt healing of the sinus and the patient left the hospital in good condition.

The patient was seen again in March 1944, with right-sided pain and pyuria and in generally poor condition. After a period of medical treatment she underwent cystoscopy. The function of the kidney was good and the stone was in an enlarged upper major calyx. At operation the kidney was high and moderately adherent. The stone was removed through an incision over the calyx and the area oversewn. The upper part of the ureter was then exposed. It was imbedded in a mass of scar tissue and markedly angulated. The ureter was dissected free and straightened out. The patient was discharged on the 17th postoperative day with a dry wound. One month later the ureter was dilated easily.

In April 1957, the patient was seen with right-sided pain. There was nausea but no vomiting, dysuria or frequency. Urinalysis, including bacteriological culture,

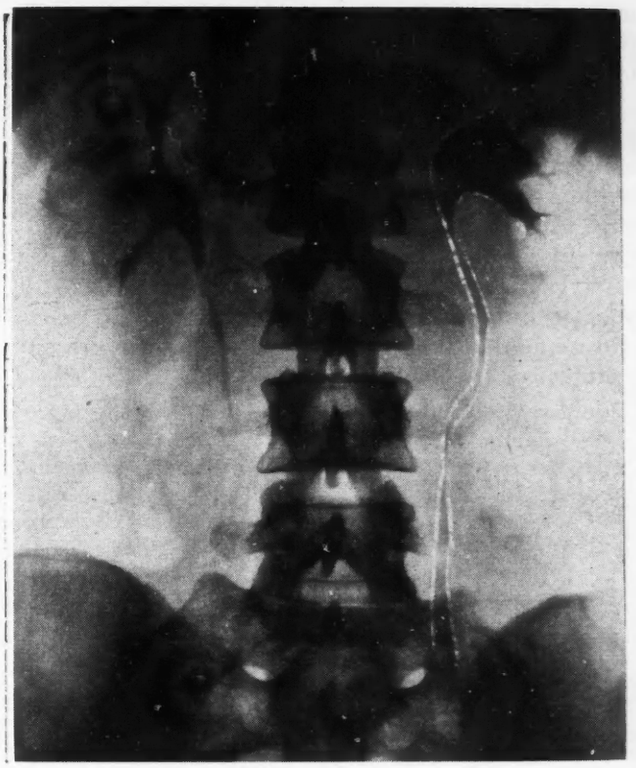

Fig. 1

was negative. None of these findings suggested a urinary condition, but with her old history, the temptation of urological study could not be resisted. Kidney function was excellent. *Radiological report*: "Both kidneys show a prompt excretion and good concentration of the dye. No significant abnormality of the left renal pelvis or calices is again demonstrated. There is again evidence of a marked narrowing and irregularity of the right upper major calyx, associated with marked dilatation of the corresponding right upper minor calices. No other abnormality of the right pelvocaliceal system is demonstrated. No additional useful information is provided." (See Fig. 1.)

COMMENT

Foulds and Varey[2] report in their article that their cases and those that they reviewed all occurred in men. This case was in a young married woman recently confined. In most of these cases, the ureter had ruptured at the site of stone. Winsbury-White[1] suggests that even where the extravasation is around the kidney the rupture will occur in the pelvic portion of the ureter.

In the present case the guilty stone was in the lower ureter but the intravenous pyelogram showed the leakage to be in the upper ureter just below the level of the lower pole. This location was confirmed in the second operation, when the adhesions around the upper ureter were definitely localized.

One can only speculate on the sequence of events in this particular case. We are all familiar with the trauma to a ureter caused by a stone, as shown by the finding of blood in the urine. We are also familiar with the problem of long-standing impaction of a stone in the ureter. Many of these stones

have to be removed by sharp dissection. Our patient had just been confined. It seems reasonable to assume that her stone had been in the upper ureter for some time and that the postpartum changes in the ureter allowed it to descend. When it became impacted near the bladder, the resulting tension caused the already damaged ureter to give way. An interesting observation of the last pyelogram is the good condition of the ureter. The cavity which held the stone in the upper calyx still persists, draining by a small channel into the pelvis and remaining uninfected as shown by the present cultures.

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Special Article

THE MEDICAL RESOURCES OF THE WORLD HEALTH ORGANIZATION

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INTRODUCTION

IN THE World Health Organization growth of international co-operation in medicine is a significant and encouraging phenomenon. The Organization has a relatively small structure and staff, yet countries everywhere are obtaining from it a wide variety of assistance in the development of their medical services. Especially significant is the growing association with official and voluntary bodies. In thus mobilizing medical resources in the interests of international health co-operation, WHO has used various methods, some traditional and tried, others novel and experimental.

POLICY PRINCIPLES

A single principle explains most of the methods in use. The governments of the world, in establishing the World Health Organization, decided that they wanted an inter-governmental body and not a supra-governmental body. The Constitution of the Organization also significantly calls for co-operation not only with official bodies whether international or national, but with non-governmental groups.

Relevant decisions of the governing bodies, i.e. the World Health Assembly and the Executive Board, are those which require WHO to design its programs for the "strengthening of local services", and to assist each country to secure at least a nucleus of health and medical staff through a system of technical education.

The basic concept of "strengthening national administrations" in the WHO system of advisory services to governments is important. It has had much influence on the methods of obtaining technical staff and facilities.

In that it is an international organization, the principle of equitable geographical distribution of origins of staff has been repeatedly declared by the Health Assembly and the Executive Board. A final matter of importance in determining the method of developing its technical resources is the relationship WHO has with other groups. This calls for much effort to secure wise co-ordination and to avoid unnecessary proliferation and overlapping of programs. Its association with non-governmental bodies gives it a most convenient and even fortunate means of obtaining authoritative technical opinion. A fuller account of these basic principles has been given in another paper.[1]

THE WORK DONE

The medical resources used by WHO for example in 1956 were to provide the following:

(a) World technical services on behalf of all countries, including the collection of epidemiological data; development of classifications of diseases and causes of death; biological standards; supervision of international quarantine arrangements; the establishment of international pathological and bacteriological reference systems; the preparation of recommendations on laboratory procedures; and the distribution of WHO technical publications.

(b) Direct assistance to governments. In 1956, WHO undertook through its regional offices 482 projects (exclusive of fellowships), in 127 countries throughout the world. These covered the whole field of medicine and health.

THE USE OF TECHNICAL RESOURCES

The main purpose of this paper is to show how in 1956, as a typical year, this geographically wide-flung and technically comprehensive program drew on medical resources everywhere. These resources were used in complete accordance with the fundamental principles described above. Indeed it was these principles which determined WHO to mobilize skills and assistance from a variety of existing country services and institutions rather than to create a large permanent organization of its own institutions and staff. However, a nucleus of its own regular staff is essential.

(a) Regular staff

In its seven offices (Headquarters and six Regional Offices), WHO employed as at December 31, 1956, a staff of 176 medical and related scientists and practitioners. These came from 40 countries. The regular staff has the responsibility of preparing, supervising and co-ordinating the programs authorized by the World Health Assembly. It also provides WHO with much of the technical knowledge, skill and experience it needs. Coming from so many different regions and cultures, it contributes valuable guidance on conditions in most regions. This helps to ensure

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acceptable and realistic programs suitable for the countries seeking WHO help. Mere technical and administrative qualifications, divorced from an awareness of regional and country circumstances, are insufficient to give sensible direction to the work of WHO or any other international agency.

Among the 176 technical members in 1956 were many who had previously held distinguished appointments as professors in universities, directors of research laboratories, clinical consultants, and medical administrators.

The development of the medical resources of the world by WHO is not to be found in its use of regular staff only. It is rather in the mobilization of available resources of the countries of the world. Resources used by WHO include temporary consultants, advisers and demonstrators; medical laboratories for inclusion in a number of world networks and reference systems; medical schools and services in education and training of WHO fellows and groups; medical and health experts convened in a wide range of advisory technical meetings and the live association of technical and professional organizations in its work. Short notes of how such medical resources are developed by WHO in the service of world medicine and health follow.

(b) Consultants, advisers and other temporary technical staff

The temporary technical staff for project field work, for short-term consultantships, and for group training schemes demonstrates especially the comprehensive arrangements for drawing on suitable talent from everywhere.

In 1956, for example, WHO had the skilled services of 232 senior advisers, consultants and demonstrators, for periods varying from days to the whole year. Through arrangements made and supervised by the WHO Regional Offices, these temporary staff members went to 127 countries and territories to assist in a wide range of medical and health activities. Communicable disease was high on the list, calling for consultants and demonstrators for malaria, tuberculosis, treponematoses and many other conditions. Nursing, nutrition, laboratory organization, virology, zoonoses, sanitary engineering and statistics, were all included.

The aspect of special interest in the present context is, however, that this impressive number of senior medical scientists and other helpers came from no less than 38 different countries. For 127 countries and territories to be aided by willing medical and health people from 38 countries is a striking pattern of exchange, diffusion and enlargement of medical knowledge. Even admitting the fact that 56% of the 232 came from only six countries, it is still impressive that 38 countries were able to supply skilled people for this international medical and health program. Many diverse cultures and types of experience were therefore found in the group, a most encouraging sign of the truly international and widespread character of these programs.

These people gave doubly to the countries in which they worked and to international development. There was their direct technical work, but inevitably much else was frequently gained by the communities receiving them. Distinguished scientists and experienced public men bring knowledge of affairs of other lands. They are stimulating; they make friendships in wide circles and come to be the source of much general knowledge and advice; they are accepted usually on returning to their own countries as interpreters, and even informal advisers and liaison officers, of the communities they have served.

One of the satisfying rewards of using temporary staff of the kind mentioned here to undertake WHO work in countries, whatever disadvantages there may be, is that all three components benefit. The country receiving the visiting consultant or adviser gains the direct value of his expert advice. The consultant invariably declares that he returns to his own service or institution with an enlarged experience and understanding, not only of more geography and culture but of his own special medical subject. WHO gains from having discharged a duty in helping a country and from enriching the general store of knowledge.

(c) The fellowship system

In 1956, consultants and advisers went from one set of countries to help those of another group. During the same period a flow of postgraduate fellows was taking place in the opposite direction. These, numbering 904, came from 109 territories and went to study in 82 countries. This is another significant way in which WHO in its annual programs draws upon world medical resources. The large number of countries offering training facilities is again perhaps surprising. This, in part, reflects the opinion of the World Health Assembly that countries should be encouraged to establish and develop their own educational institutes at which international courses may be held. WHO assists such institutes in various ways.

As indicated in the special study of the program of education and training made in 1953, WHO is continuing and expanding fellowship methods first evolved and practised by such bodies as the League of Nations Health Organization, the Rockefeller Foundation, and others.[2]

It is important that in recent years fellowships have been linked with appropriate projects in the fellows' own countries. The WHO regional system is an effective means for operating such an arrangement.

The fact that 82 countries are members of the world-wide system for training WHO fellows reveals how wide a range of institutions, experience, culture and language is open for selection. This, in part, reduces some of the difficulties of training shown in earlier schemes. The fellow is able now more readily to find training and circumstances, including cultural and language needs, appropriate to prepare him for a contented return to work in his own country. The institutions (hospitals, laboratories and medical schools) and services (central or local) providing the training also have fewer problems of co-operation. In outlook, experience and language, fewer unsuitable fellows are received.

It is a rich association in which many country and local institutions join. Besides the satisfaction

of helping postgraduate men and women from many lands, they secure a wealth of interest and advantage. Thus develop links and exchanges covering the world. There are now few universities, schools, laboratories or services outside the WHO fellowship system. An enormous fund of wisdom and experience is thus at hand for training doctors and scientists of all countries. These institutions generously open their facilities to WHO fellows, usually without any special subsidy although a few are assisted to provide suitable international courses.

(d) Advisory committees and meetings

The committee, conference or other form of gathering is even more prominent in international than it is in national life. Partly by chance and partly by design, there are two broad types of WHO advisory technical meetings. There is, firstly, a formal arrangement of expert advisory panels and committees governed by Executive Board regulations. These continue the basic work of the previous commissions and committees of the League of Nations on, for example, pharmacopœias, biological standardization and nutrition. The panels supply WHO with technical advice by correspondence and provide the membership of its expert committees. In 1956, there were 34 panels covering the following subjects:

Addiction-producing drugs
Antibiotics
Biological standardization
Brucellosis
Cholera
Chronic degenerative diseases
Dental health
Environmental sanitation
Health education of the public
Health laboratory methods
Health statistics
Insecticides
International pharmacopœia and pharmaceutical preparations
International quarantine
Leprosy
Malaria
Maternal and child health
Mental health
Nursing
Nutrition
Occupational health
Organization of medical care
Parasitic diseases
Plague
Professional and technical education of medical and auxiliary personnel
Public-health administration
Rabies
Rehabilitation
Trachoma
Tuberculosis
Venereal infections and treponematoses (including serology and laboratory aspects)
Virus diseases
Yellow fever
Zoonoses

The panel is proving a useful means of access for WHO to both scientists and their institutions, and hence to up-to-date work and opinion throughout the world. It is a simple, direct and efficient method for obtaining technical advice and guidance for any feature or project of the WHO activities. The panel is again a two-way channel of information. Its members both give and receive and even combine in the diffusion and extension of knowledge in their subjects. Such members for the 34 panels in 1956 numbered 1491 and resided in 67 countries. This is yet another striking example of the determination to tap all possible sources of information.

In their second role of providing the membership of the WHO Expert Advisory Committees, 14 expert committees were attended in 1956 by 112 panel members from 35 countries. The reports of such meetings are usually published in the WHO Technical Report Series. Thus this series portrays a corporate technical opinion compounded from world-wide resources as represented in experts from many countries. A fundamental principle to note is that the reports represent the actual opinion of the experts. The WHO regulations in question state that "the text of a report of the committee may not be modified without the consent of the committee by which it was drawn up".

The second arrangement of advisory technical meetings is less formal and definite. It includes a variety of study groups, consultant meetings and similar arrangements. The membership is similarly less formal and includes *ad hoc* invitations to individual scientists, whether members of expert panels or not. This series of meetings merges into the bigger and broader form of conference, where the purpose is occasionally more educational for the members than advisory to the Organization. In addition, a number of seminars were held during the year. Complete statistics are not available for the 33 meetings of this kind held during 1956. These were convened in countries in Africa, the Americas, Europe, Western Pacific, South-East Asia, and the Eastern Mediterranean. Scientists from almost all countries were included in the total membership, which came to over 500 scientists and health workers—yet another demonstration of a comprehensive pooling of resources.

Whatever weaknesses exist in the use of committees and similar bodies in supplying decisive, clear, technical opinion, there are undoubtedly many advantages in the system. As used by WHO, it is a simple international means of securing corporate and even authoritative opinion reflecting an assessment of many factors frequently beyond adequate consideration by a single local or national group.

(e) Local medical institutions and WHO

It is clear already that the WHO policy of seeking much of its technical needs from sources in countries rather than in creating its own internal institutions means the incorporation in its work of numbers of local medical and health institutions—laboratories, medical schools, hospitals, etc. Some WHO methods in thus marshalling medical resources may be described.

There is a whole series of laboratories scattered over the world which form part of various international networks organized by the Organization, or which individually act as general reference centres. Some have much useful history and tradition already behind them. The reference centres for biological standards, in London at the National Institute for Medical Research and in Copenhagen at the Statens Seruminstitut, were set up by the League of Nations. The international shigella, salmonella and escherichia centres distributed between Atlanta (Georgia, U.S.A.), London and Copenhagen, represent a useful initiative by a non-governmental group—the International Association of Microbiological Societies—its arrangements being taken over at the appropriate stage by WHO.

The best known of the laboratory networks are those associated with influenza and poliomyelitis

virus research and exchange of information. The former are related to the World Influenzal Centre in London and to the International Influenzal Centre for the Americas, Montgomery, Alabama, and the latter to a number of regional centres now being established in certain local laboratories.

The use of existing laboratories in countries for such world reference, exchange and similar co-ordinated research purposes covers many other subjects, such as medical statistics, blood grouping, authentic chemical substances, typhoid vaccines, brucellosis, rickettsiosis, bilharziasis, cholera, rabies, plague, yellow fever, treponematoses, trachoma, onchocerciasis, nutrition, insecticides, and other subjects.

The more formal and traditional association has been recognized by a system of agreements between WHO and the individual countries whereby the Organization pays annual grants of a moderate size to the institutions assisting in this international work. In the large number of other arrangements, some experimental, others only temporary, WHO also assists in various ways, sometimes by grants or by exchange systems or essential technical supplies.

This method of drawing upon local medical institutions, especially laboratories, for world-wide programs of co-ordinated research has become one of the most significant WHO activities. It has resulted in well over a thousand national and local institutions becoming partners in and contributing their resources to international medicine and health.

It is promising even wider opportunities. Shortly one of its most potentially useful applications is to be made. Following the proposals in 1955 of a consultant group on WHO Cancer Programs[3] and an Executive Board recommendation in 1956,[4] a pilot scheme for an international pathological reference centre is to be launched in 1958. In this a suitable local centre will hold selected pathological tissues available for reference and distribution to assist in the definition and co-ordination of research work, especially epidemiological, in different countries on such subjects as various neoplasms, malnutrition, blood diseases and parasitic diseases. No finer service could be offered by WHO to medical research in many subjects and no more simple and efficient means secured for incorporating research institutions everywhere in a world service.

(f) *Non-governmental Associations*

It is fortunate that both the WHO Constitution and the early policy decisions of the Health Assembly and the Executive Board gave full scope for associating non-governmental and unofficial groups in international medicine and health. Rich sources of initiative, goodwill, skill and experience, reflecting much useful variety and many local relationships, exist in these groups.

The first years of WHO's life have seen numbers of such groups joining in both formal and informal arrangements from which the Organization has drawn many advantages. There are such great professional and technical bodies as the World Medical Association, the International Unions against Cancer, Tuberculosis, Venereal Diseases and Rheumatism, the World Federation for Mental Health, the International Dental Federation, the International Council of Nurses, the League of Red Cross Societies and many others, to a total of 40 in formal relationship. Numbers of others in various *ad hoc* ways have also assisted many WHO programs. These groups, with their substantial professional and scientific standing and wide range of contacts, have given WHO and international medicine and health access to funds of goodwill and specialized knowledge everywhere.

The non-governmental groups assist international medical and health programs in a variety of ways. Many of them have submitted reports to WHO giving surveys of the subjects they have studied. They have taken part in consultant and study groups contributing technical direction of international proposals. Some play an essential part in the operation of world technical standards, networks and centres. Most supply valuable data and conversely have assisted in distributing information about WHO arrangements and programs.

THE FINANCIAL RESOURCES

The year 1956, for which the essential reports are available, may be taken as typical of the programs at present being undertaken by WHO and of the way it draws on world resources for its purposes.

TABLE I.

	Purpose of appropriation	*Obligations*
		U.S. $
Part I.	*Organizational meetings*	
	World Health Assembly	188,434
	Executive Board and its Committees	105,719
	Regional Committees	57,782
	Totals—Part I	351,935
Part II.	*Operating program*	
	Central Technical Services	1,564,122
	Advisory Services	5,464,156
	Regional Offices	1,459,217
	Expert Committees and Conferences	120,208
	Totals—Part II	8,607,703
Part III.	*Administrative Services*	
	Administrative Services	1,023,156
	Totals—Parts I, II and III	*9,982,794

*Off. Rec. WHO No. 78, Financial Report 1956, Extract from p.13.

The World Health Assembly appropriated an amount of U.S. $12,074,144 for this financial year, of which an amount of $10,203,084 was to finance the direct activities of the Organization for the year.[5] The balance of $1,871,060 was appropriated to an undistributed reserve. In the outcome the obligations incurred for the year were those given in Table I.

In addition, during 1956 WHO participated in the United Nations "Expanded Program of Technical Assistance for Economic Development" and

incurred expenditure, which was met from UN sources available for this purpose, to an amount of U.S. $5,450,454. These funds were expended as follows:

Direct project costs	$4,843,844
Operational services costs	386,927
Administrative costs	219,683[6]

Its sources of funds also included an amount of U.S. $112,058 received from the United Nations Children's Fund towards the technical participation of WHO in a variety of programs undertaken during 1956.[7] This was quite apart from the large sums distributed by UNICEF for medical supplies and equipment used in jointly assisted country programs.

In effect, WHO therefore used financial resources of just over U.S. $15,500,000 in this year to maintain its administration and carry out its wide variety of technical programs throughout the world. This statement is a general one in that it deals with direct functions of WHO and omits certain combined activities financed by other funds, including those of the Pan-American Sanitary Organization. Such activities, though financed by these other bodies, in part used certain WHO facilities.

FINAL REMARKS

This paper has given an outline of the methods developed by WHO in terms of its constitution and policies to obtain the medical resources it needs for its work. It has secured and applied these by using a relatively moderate-sized organization incorporating regional offices, and spending a sum of modest proportions.

The present examination of the methods of WHO shows that the basic principle has been followed of seeking assistance in existing country and local services and institutions in preference to constructing new WHO systems of its own staff and institutions.

The Organization has extended the arrangements it inherited until today in less than ten years of development these cover practically the whole world and all medical and health subjects. It is a flexible, living system in which the majority of the leading medical practitioners and institutions of the world are the essential components. These are the storehouses of modern medical knowledge. A simple system of association and co-operation is enabling WHO to draw on them in conducting its world-wide services on behalf of the world's governments. Without exception these local and national services have responded readily to join in international co-operative technical programs. Thus their talents, traditions, experience and ingenuity are serving not only their own communities but all mankind. A wider purpose is being given them. This greater responsibility brings its reward. The medical people and institutions who give their services to other countries and to international programs gain in experience and enlarge their association, including the international recognition granted to them in such work.

This world-wide system of arrangements by which so much of the world's medical resources are used is complicated. It has certain weaknesses. Its efficiency is not uniform. Many of its methods are still experimental. Nevertheless, in a relatively short time it has become a partnership of independent trained minds and institutions in a service co-ordinated and supervised by WHO by which the world is given the best of medical knowledge and guidance.

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SHORT COMMUNICATIONS

PROPOSAL FOR A CERTIFIED STANDARD FOR USE IN HÆMOGLOBINOMETRY—SECOND AND FINAL REPORT*

[The March 15, 1955 issue of this Journal contained an item in the section on "Clinical and Laboratory Notes" in which the need for standardization of methods for use in hæmoglobinometry was stressed. A committee was formed for investigation of the question and was made up of members of the Division of Medical Sciences of the U.S. Academy of Sciences and the National Research Council of Canada. Prominent American hæmatologists and pathologists were appointed; Canada was represented by Dr. A. H. Neufeld. Highlights of the final report of this committee are now given in condensed form.]

MOST ROUTINE methods of clinical hæmoglobinometry depend upon the photometric measurement of a blood sample after quantitative conversion of the hæmoglobin which it contains into one or another of its derivatives. For the standardization of such a procedure there is needed a colour standard which, when measured in the photometer and cuvette in routine use, will establish the relation between instrument reading and concentration of the particular hæmoglobin derivative. This relation can then be used in converting instrument readings for unknown samples of blood to concentration of hæmoglobin by the use of Beer's law or by construction of a calibration curve.

In the opinion of the Panel, the most significant contribution which could be made to the refinement of clinical hæmoglobinometry would be the widspread adoption of a single method of analysis.

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Failing this, the indirect calibration of other methods with the chosen method offers the only simple photometric means for the comparison of data. The procedure, however, is subject to error if the blood sample contains significant amounts of certain of the abnormal forms of hæmoglobin. For example, methæmoglobin and carbon monoxide-hæmoglobin are quantitatively convertible to cyanmethæmoglobin, but not to oxyhæmoglobin.

The Panel reviewed the several photometric methods in current use and came to the conclusion that the procedure involving the measurement of hæmoglobin as cyanmethæmoglobin was the most promising. It offered the following advantages: (1) simplification of the procedure calling for the use of a single reagent;[1, 2] (2) adoption of this method by the U.S. Army after extensive field trials;[3] (3) applicability to all forms of hæmoglobins except in sulphæmoglobinæmia; (4) suitability for measurement in filter-type photometers and narrow band spectrophotometers; (5) stability of standard cyanmethæmoglobin solutions when properly cared for.[3]

A preliminary report of extensive trial of these standard solutions was published in 1955.[4, 12] This report outlined recommendations of the Panel, described arrangements for the preparation and distribution of certified standard solutions of cyanmethæmoglobin, and invited co-operation in an extensive field trial of the use of the standards and of the recommended method of analysis.

More than a thousand laboratories volunteered to co-operate in the trial sponsored by the United States National Research Council. Distribution of the standards was made with the assistance of the College of American Pathologists, the National Association of Clinical Laboratories, the Walter Reed Army Institute of Research, and the National Research Council of Canada. The laboratories received not only descriptions of the procedures for the use of the standards to calibrate photometers, but also directions for the routine determination of hæmoglobin in the form of cyanmethæmoglobin.

The results of the study were most gratifying. The need for, and the ready and grateful acceptance of, a simple method for the standardization of hæmoglobinometers was apparent. The recommended method of analysis was likewise well received. At the onset of the field trial study only 7% of the co-operating laboratories had been determining hæmoglobin as cyanmethæmoglobin. At the time of the last report, two-thirds of the co-operating laboratories were using this method.

In the first field trial, the standard solutions were prepared from crystalline hæmoglobin by Dr. David Drabkin. Three solutions in carefully determined concentrations of approximately 60, 40 and 20 mg. of hæmoglobin per 100 ml. were distributed. The optical densities of the final solutions were independently confirmed and a continuing control on stability was maintained in the laboratories of Dr. Brecher, Mr. Gould, Col. Crosby, Dr. King, and Dr. Neufeld. Agreement having been reached on the optical density values, the hæmoglobin concentrations of the standards in mg. per cent were computed from the optical densities, assuming that the extinction coefficient of cyanmethæmoglobin per milligram-atom of iron per litre is 11.5 and that the pigment contains 0.335% iron.

Two problems were encountered during the course of the field trial study. The first of these was the growth of certain micro-organisms observed in some samples in spite of the presence of cyanide. This made it necessary to prepare and to maintain the solutions under sterile conditions. The second problem was a change, unpredictable in degree and not reported by all checking laboratories, of 2% to 6% in the optical density six to nine months after distribution of the standard. Samples from each lot were found to have undergone varying degrees of change, mostly fading, which was compensated in some samples by a comparable increase in turbidity. The standards prepared and distributed by the U.S. Army in its earlier field trial had remained unchanged in optical density for three years. Inasmuch as these solutions had been prepared directly from whole blood or from washed red cells, it was suspected that the manipulation involved in the preparation of the crystalline hæmoglobin for the National Research Council standards might have reduced the stability of the pigment. Therefore, a new standard was prepared from washed cells. The new standard was further modified by increasing the concentration of cyanide, since some previous preparations with such higher concentrations had shown greater stability and since the growth of most organisms would be limited by the higher concentration of cyanide.

Since the percentage change in optical density of the first standards was greater with increasing dilution of the hæmoglobin pigment, and since cyanmethæmoglobin solutions follow Beer's law, the second standard was distributed in only the most concentrated (60 mg. % of hæmoglobin) of the three dilutions.

The second group of standards, modified as outlined above, was distributed in July and August of 1956. Their stability was determined in the laboratories of Dr. Drabkin, Dr. Brecher, Mr. Gould, and Col. Crosby. The stability was satisfactory for at least nine months from the time of preparation, no change of more than 2% in optical density being observed.

The members of the Panel have concluded that solutions of cyanmethæmoglobin, when prepared, calibrated and handled properly, are acceptable as standards for hæmoglobinometry. They recognize that such standards are not ideal in all respects. However, until better standards can be developed, they are of the opinion that the availability of this reagent will greatly simplify the calibration of

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hæmoglobinometers and will greatly increase the accuracy of hæmoglobinometry over previously employed practices.

Finally, they encourage further independent investigation in the hope that an even better standard may be developed, particularly one with improved stability and more certain maintenance of sterility.

The National Research Council supplies of the standard cyanmethæmoglobin solution are now exhausted and no further production is planned under the auspices of the Academy-Research Council. However, standards are now available from several commercial sources. The NAS-NRC has recommended the establishment of a program of certification of commercially produced cyanmethæmoglobin standards to determine conformance with the specifications it has established. In response to the need for the establishment of such a program, as defined by the NAS-NRC, the College of American Pathologists has arranged for certification through the facilities of the laboratory of the American Medical Association in Chicago. On the basis of data obtained through this laboratory, the College of American Pathologists will certify whether commercially produced standards which have been submitted comply with the specifications established by the NAS-NRC. *All users are urged to insist that the cyanmethæmoglobin standards they purchase commercially carry the certification label of the College.**

Detailed instructions for the preparation of the standards have been published by Crosby.[13] Producers of the standard or instrument manufacturers may obtain technical details on the adaptation to and use of the standard in the various hæmoglobinometers by writing to the Division of Medical Sciences of the National Research Council.

The final recommendations of the National Research Council *ad hoc* Panel on the Establishment of a Hæmoglobin Standard are as follows:

1. That cyanmethæmoglobin be adopted as a standard in clinical hæmoglobinometry.

2. That the standard be characterized spectrophotometrically on the basis that the extinction coefficient of one milligram atom of iron (c= 1 mg. atom of iron per litre, d= 1 cm.) in the form of cyanmethæmoglobin at a wavelength of 540 mμ is 11.5.

3. That 0.338% (w/w) be accepted as the iron content of hæmoglobin (molecular weight of 16,520 per gram atom of iron) in accordance with the recent recommendation of the Protein Commission of the International Union of Pure and Applied Chemistry, and that a factor of 1652 be used in calculating hæmoglobin in mg. per 100 ml. from millimoles per litre.

4. That the standard be distributed as a single concentration of not less than 55 mg. of cyanmethæmoglobin per 100 ml.

5. That solutions be distributed in brown glass bottles and in sterile condition.

6. For the present it is recommended that solutions should be used as standards for a period not to exceed nine months from the time of preparation. This dating period is based upon the results of the National Research Council field trial. As experience accumulates with commercially prepared samples, an extension of the dating period may well be found to be justifiable.

7. That the standard be prepared from either crystalline hæmoglobin or washed erythrocytes.

8. That commercial producers of the standards submit representative specimens from each lot to the College of American Pathologists, Prudential Plaza, Chicago 1, Illinois, U.S.A., for certification:

(a) that the concentration of cyanmethæmoglobin is within ± 2 per cent of the value stated on the label;

(b) that the solution is substantially optically clear; and

(c) that it is microbiologically sterile.

*In Canada discussions are now taking place in order to make one national laboratory responsible for the production and certification of the standard solutions.

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PORTABLE PROJECTION TABLE FOR 2″ x 2″ AND 3¼″ x 4″ SLIDES

ARTHUR SMIALOWSKI,* *Toronto*

THIS SIMPLY CONSTRUCTED projection table is well suited to hospital use, when it is necessary to project slides of many sizes and in more than one location.

The table, which is 5′ long and 1′ wide, is constructed mainly of plywood, that of the sides being 1″ in thickness, the back ¼″ and the front, which contains two drawers each measuring 4″ x 18″, being ½″. The lower shelf and the top are of ¾″ plywood, the top having a railing 1½″ in height. The elevation upon which the 2″ x 2″ projector stands is made of ¾″ plywood, and the whole is complete with a natural stain finish. The four hard rubber castors are each 2″ in diameter.

On either side is a hook upon which the electrical cords may be hung. The electrical installation is of heavy insulated wire, ¼″ in diameter, with two outlets—one for the 2″ x 2″ projector, and one for the 3¼″ x 4″ projector.

*Chief, Photography Department, St. Michael's Hospital, Toronto, Ont.

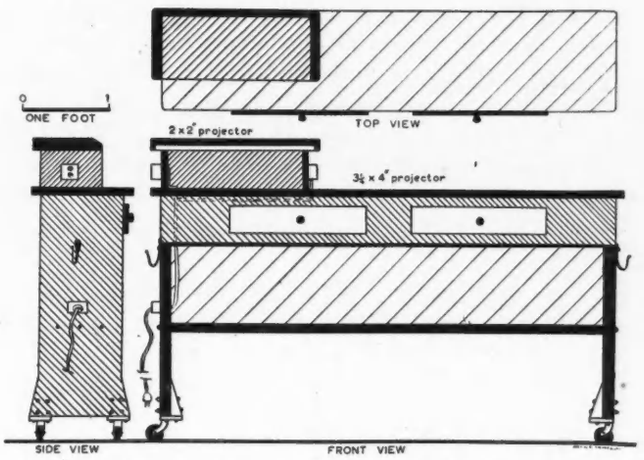

Fig. 1.—Diagram showing projection table construction in three views.

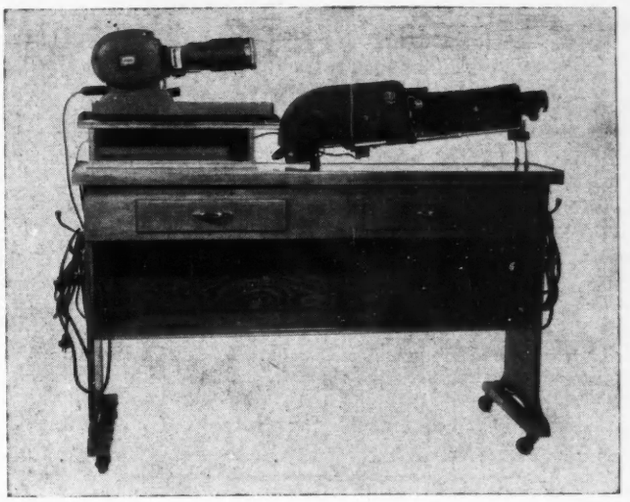

Fig. 2.—Photograph of projection table complete with projectors.

The 2″ x 2″ projector, shown in Fig. 2, is a "Leitz Prado 500", with "Hektor" 200 millimetre focal length lens, and can be adapted to film strip projection. The 3¼″ x 4″ projector is a "Spencer Delineascope", Model GK, with "Bausch & Lomb" 381 millimeter lens. This projector has interchangeable slide carriers to accept 2¼″ x 2¼″ and 3¼″ x 3¼″ slides as well as the 3¼″ x 4″ size slides. This lens combination will project 2″ x 2″ and 3¼″ x 4″ slides to approximately the same picture size on the screen.

The features of this projection table are: it can be easily constructed by a carpenter; it can be moved from place to place without difficulty; it carries extra extension cords, bulbs, test-focusing slides, etc. This unit has proved very useful since its construction two years ago.

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MEDICAL CERTIFICATION

The advent and development of insurance against sickness in the western world has confronted physicians in many countries with problems of medical certification. These problems are not yet acute in North America where most workers have every incentive to remain at work and the rewards for idleness tend to be minimal. But where the welfare state exists, voices are not infrequently raised to suggest that some medical certificates of unfitness are much too readily granted. For example, in Britain it has been suggested that, because of the pressures put upon them by patients, practitioners are apt to be overgenerous with certification. If they do not adopt this attitude, it is easy for the patient to change his doctor. The practitioner will answer this accusation by saying that though unmistakable signs of disease are recognized in the textbooks, there are unfortunately no infallible signs of perfect health. If a patient comes to his physician and claims that he is unfit for work, it is almost impossible for the practitioner to prove that he is making an untrue statement.

This is an aspect of medical practice about which few figures are available. It is therefore interesting to read an article by a Lancashire practitioner, who analyzed the medical certificates issued in his practice during a period of twelve months. The general practitioner, Dr. Ashworth (*Lancet*, 1: 732, 1958), was in a rather special type of practice with 3300 patients, forming part of a health centre established by the University of Manchester as an experimental teaching centre. His average number of items of service per year given to each patient is four.

Ashworth analyzed his certificates under three headings: (1) unjustified claims; (2) justified claims; (3) chronic sick. He affirmed that during the year 457 men and women made 555 claims and drew £7878 (about $21,000) in benefit. He found that in his practice there were ten obvious malingerers, to all of whom certification was refused. There were, however, a group of 44 women and 54 men to whom certificates were issued although the doctor felt that they were expanding their absenteeism beyond the time strictly necessary on medical grounds. This group of 98 patients cost the insurance scheme £410 (about $1100), i.e. about 5% of the total money paid in benefits, and amounted to about 20% of all claimants for money.

The figures also show the immense drain on insurance funds made by the chronic sick; although in this practice the group consisted only of 15 women and 17 men, none of whom were very likely to resume work again, they drew as much money from the funds as all the short-term absentees put together.

From these figures Ashworth makes two points. The first concerns the chronic sick. He wonders whether it would not be a good thing for patients who have been sick for more than a year to change their doctor, since the regular doctor is liable to become apathetic about their prospects of recovery. He notes that these chronic sick often become sullen and suspicious, believing that they are regarded as malingerers. The community would be justified in spending large sums if necessary to prevent their reaching this stage, at which disablement resettlement officers and other rehabilitation agencies have a difficult task.

The other point that he makes concerns certification for social and domestic circumstances. In his category of unjustified claims, he found a few men and women who though not actually ill were placed in a social or domestic dilemma which required a short period of absence from work. He cites the case of a man who had to stay off from work to look after two sick children. The easiest way to prevent the man from losing his job in these circumstances is to issue a medical certificate. Clearly this is a difficult situation and involves a fine point in medical ethics. One wonders whether issuing what is certainly a false certificate on medical grounds is justified because it is the easiest way out of the dilemma, and does the least harm in the long run to the community. These doubts are evidently shared by an editorial writer in the same issue of the *Lancet*, who feels that it would be better to arrange for medical certifications on social or emergency grounds. Again one wonders whether it is the physician's job to act as a welfare officer and arbitrate in social and economic fields outside the scope of medicine. For example, certain women workers may from time to time have home commitments, such as the care of the sick, which necessitate their absence from work, but it is surely no part of the physician's duties to arbitrate in such cases. These problems do not figure to any large extent in Canada at present, but they loom on the horizon. It is encouraging to feel that in a welfare state system such as that of Great Britain, the abuses are apparently not as great as the pessimist would suggest.

Editorial Comments

SPIRAMYCIN

Spiramycin is the name approved by the British Pharmacopœia Commission[7] for an antibiotic agent produced by *Streptomyces ambofaciens*. It is also known as Rovamycin(e). Spiramycin has pharmacological, therapeutic, and toxicological properties which are in general similar to those of erythromycin.

Streptomyces ambofaciens was isolated from a sample of soil obtained in the north of France.[27] The species was given its name from the fact that it makes two antibiotics, spiramycin and a trypanocidal agent, congocidin.[12] Spiramycin is extracted from the culture medium at pH 9 with organic solvents such as amyl acetate. It is a pale, cream-coloured, amorphous base, with a bitter taste and almost insoluble in water. The base is capable of forming water-soluble salts, such as the sulphate and adipate. The base is a mixture of three components, two of which appear to be of a similar nature.[27]

Spiramycin is available for clinical use as capsules, each containing 250 mg. of the base. The recommended dose is two to three capsules every six hours.[27, 29] This corresponds to approximately 0.05 g. per kg. body weight per day. The dose is about twice that of erythromycin.

Studies upon the completeness of absorption of spiramycin from the gastro-intestinal tract have not been published. Samples of blood taken one hour after oral administration of 12.5 mg. per kg. of spiramycin contain in the order of 1 microgram per ml. of the antibiotic, which is about the same level produced in the same interval by 6.25 mg. per kg. of erythromycin.[22] Blood levels of spiramycin are maintained at peak values for four to six hours.[19] The concentration reached in the cerebrospinal fluid is two-thirds that in blood.[15] The antibiotic is eliminated rather slowly and traces may be present in blood 24 hours after oral ingestion of a dose of 2 g.[15] Large amounts are excreted in bile and presumably reabsorbed, and about 10% is eliminated in urine.[15] More rapid elimination has been reported following intramuscular injection,[14] which suggests that prolonged elimination may be due to prolonged absorption from the intestine.

The antibacterial spectrum of spiramycin *in vitro* is similar to that of erythromycin.[13-15, 17, 22, 24, 27, 30, 31] Higher concentrations of spiramycin are necessary to inhibit bacterial growth in cultures,[16, 20, 26, 28] possibly because the antibiotic action of spiramycin is delayed.[37] *In vivo*, experimental infections of animals respond about equally well to erythromycin and spiramycin.[11, 14, 15, 22, 27, 30] Clinically, spiramycin has been reported effective against pneumococcal infections,[13, 15, 25, 31, 34] staphylococcal infections,[13, 15, 30] streptococcal infections,[13, 15] enterococcal infections,[13, 15, 30] syphilis,[15] gonorrhœa,[15, 35, 39] non-gonorrhœal urethritis,[38] intestinal amœbiasis,[10] exanthematous typhus,[15, 31] and lymphopathia venereum or Nicolas-Favre disease.[21, 23] In instances where an estimate was made of the relative clinical effectiveness of spiramycin, erythromycin, penicillin and the tetracyclines, all antibiotics were reported of approximately equal value.[18, 19, 21, 34, 38] Spiramycin has been found clinically ineffective against meningococcal meningitis,[31] typhoid fever,[31] pneumonia due to *Klebsiella pneumoniæ*,[18, 19] infectious mononucleosis,[13] and *Trichomonas vaginalis* urethritis.[36] In addition, spiramycin has been found ineffective in mice infected with *Trypanosoma congolense* and *brucei*,[11] *Plasmodium berghei*,[11] and *Pasteurella pestis* and *septica*.[8] Spiramycin has been found active against infections resistant to penicillin[1, 15, 29, 31] and the tetracyclines.[30] It is apparently active against some strains of organisms which are resistant to erythromycin,[9, 14, 16, 18] but not against other strains.[14, 15, 22] Infectious organisms in turn develop resistance to spiramycin.[14, 15]

In acute, oral toxicity experiments upon animals, spiramycin has been given to dogs in doses up to 9 g. per kg. body weight without producing death, because the dog vomits these large doses.[3] When dogs are anæsthetized to prevent vomiting, the oral LD50 of retained spiramycin is 5.2±1.6 (mean±S.D.) g. per kg. body weight.[3] The oral LD50 in albino rats is 9.4 ± 0.8 g. per kg.,[3] and in mice is over 5 g. per kg.[11, 27] The oral LD50 in mice is about 4 g. per kg. for erythromycin and for oleandomycin.[33] Subcutaneous administration of spiramycin adipate produces local irritation at the site of injection in albino rats.[2] Clinical reports upon some 600 patients given spiramycin orally in a dose of 2 to 4 g. per day indicate that one or more of the four symptoms—diarrhœa, gastralgia, nausea, or vomiting—may occur in about 1 out of 30 patients.[1, 10, 13, 15, 19, 21, 22, 30, 32, 34, 35, 38] In the some 97% of patients who get no untoward effects from oral doses of 2 to 3 g. per day, treatment may be continued at this dosage for a month or longer without evidence of chronic toxicity.[15, 21] Chronic administration of larger doses of the order of 0.5 to 1 g. per kg. body weight per day to albino rats and dogs eventually produces a toxæmia in these animals.[4-6]

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INFANTILE SCURVY IN CANADA

Two reports in recent issues of the Journal, recording a sharp rise in the incidence of cases of infantile scurvy admitted to children's hospitals in Toronto[1] and Winnipeg[2] in recent years, reveal a situation which is both puzzling and challenging. In this day of ready availability of multivitamin concentrates and of mass saturation of the lay public with medical knowledge, it is surprising that a preventable nutritional disease, more or less consigned to clinical oblivion, should occur in such numbers. In looking about for an explanation, it is necessary to explain why this increase seems to be occurring only in certain areas.

The clinical observations of Whelan and of Grewar are very similar. The cases observed were divided equally between city and rural populations. The age incidence covered the period from 6 to 12 months. None of the infants was breast fed for more than a few days. Infection appeared to precipitate the acute clinical manifestations and led to hospital admission. It was clear that in many instances, vitamin C was not given to the infant, either as orange juice or vitamin supplement. In some it was given but refused or vomited. In a few the history was proven to be unreliable and actual concealment of the facts was revealed by both authors.

The clinical picture was a classical one and radiological findings were typical. In spite of this, in both series, most of the infants reported were referred to hospital with a diagnosis other than scurvy. This is obviously the result of lack of familiarity with the disease on the part of the physicians, many of whom had probably never before seen a case of scurvy. For this reason alone, it is important for the physician to read through these articles and become reacquainted with a disease which has done much to change the course of history.

Scurvy occurs most often in families in the lower socio-economic brackets. It is essentially, however, a disease of ignorance and not of poverty. Multivitamin preparations are useful and handy. But both doctor and patient must be sure that the product prescribed contains A, D and C vitamins and that the dosage prescribed is adequate. The pharmacist must not substitute products which may contain A and D vitamins but lack vitamin C. The multiplicity of products available can lead and has led to confusion and error in this regard. The mother must be instructed to administer the concentrate directly on the tongue or by spoon and not allow the few drops to disappear into the depths of the feeding mixture. Apparent intolerance to a vitamin concentrate should be reported to the physician.

There is a good argument for a return to orange juice. Vitamin C is remarkably stable almost no matter how orange juice is processed or stored. Neither the medical profession nor the lay public seems to be aware of this information. The causal relationship of ingestion of orange juice to infantile colic and eczema has probably been exaggerated. Its use has been discouraged in many instances on insufficient evidence.

The decline in breast feeding has played an important role in the continued occurrence of scurvy. All the cases reported by the authors were fed cow's milk. The decline in breast feeding is particularly regrettable in our native population and in the lower-income group, where the expense of vitamin concentrates may be a factor in the rise of scurvy.

Why the concentration of cases in the Winnipeg and Toronto areas? No good explanation of the peculiar geographical upsurge in the incidence of scurvy has been presented. Other cities in Canada have not had the same experience in spite of similar types of population and reasonably adequate public health and pædiatric care programs. Can it be that lack of familiarity with the clinical picture has led to missed diagnosis? If so, it is likely that the publication of these two papers will lead to increased recognition of a disease which many physicians have relegated to the dusty files of medical history.

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FINANCIAL ASPECTS OF HEALTH INSURANCE

The Canadian Tax Foundation has recently published an interesting report—"Financial Aspects of Health Insurance" by Malcolm G. Taylor.* The author undertakes an analysis of present information on the incidence and impact of illness, existing health resources and health expenditures, and the financial implications of existing and proposed government health insurance programs.

The study sets out in a logical manner a factual, authoritative analysis of a subject very susceptible to emotional consideration and warrants serious study by those interested in impending legislation. Certain of his conclusions merit comment here.

Dr. Taylor portrays an existing pattern of increases in hospitalization costs and suggests that such costs will continue to increase in the future, but at a lower rate, whether government programs are implemented or not. He attributes past ac-

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celerated increases to an unprecedented increase in bed capacity to meet a backlog requirement, to increasing utilization of existing facilities by the public generally, whether insured or uninsured, and to changes in per diem rates due to inflation, realignment of hours of work and salaries of hospital personnel, and requirements for additional personnel occasioned by advances in medical technology.

He suggests that many of these factors will assume reduced significance in the future and that increases will not continue at the same accelerated pace. Our population is expanding rapidly and indications are that we will be fortunate if net future increases in hospital beds keep pace with increases in population. Thus, an effective limiting control will be the number of available beds. He agrees that insurance, per se, creates a new demand resulting in increased utilization of services but suggests that this factor applies whether insurance is provided privately or by government. His statistics indicate that under any insured arrangement, we may initially expect substantial increases in utilization until a plateau is reached beyond which increases are minimal.

Dr. Taylor assumes increases in per diem cost to be the dominant factor in assessing long-term financial implications, but he expects that the rate of increase will not be proportional to past experience. He states that past accelerated increases in economic gains of hospital employees have brought their salaries and hours of work more nearly in line with those of comparable workers, and we may expect future increases at rates consistent with trends in the rest of our economy. Substantial increases are envisaged as a result of outside trends and changes in medical technology, but he suggests that such increases will be no greater under a government program than under existing arrangements.

A summary of his report might be simply stated as: The question is not whether we can afford government-sponsored hospitalization programs but whether we can afford the increased costs which will be associated with health services regardless of government's interest. Dr. Taylor suggests an affirmative answer. Experience indicates that as our real income has increased we, as a nation, have indicated a willingness to contribute a larger portion of our income to essential health services. He concludes that with rising incomes the public would continue to increase expenditures for health services even in the absence of a national program.

As Dr. Taylor's study is primarily a consideration of the financial implications of global expenditures for health services, certain other information is necessarily excluded. Information is listed as to methods of financing various programs but Dr. Taylor does not assess the merits of proposed fiscal policies. One would also have welcomed an assessment of the role of deterrent charges, both as an element of control and as a method of financing. We would hope that someone as familiar with this subject as Dr. Taylor will undertake such analyses.

B.E.F.

Fructosuria with Clinical Symptoms

Essential benign fructosuria is a rare condition, and like all the other less common melliturias is asymptomatic. A positive family history is sometimes obtained (Marble[1]), but the main interest in this condition has been its differentiation from diabetes mellitus.

Chambers and Pratt[2] described a case of idiosyncrasy to fructose in a 24-year-old woman. There had been difficulty in weaning her at 10 months, and she invariably reacted with vomiting to the intake of fruit or cane sugar. Her glucose tolerance test was normal; fructose tolerance test figures were just above normal. Her parents were free of symptoms or fructosuria after oral intake of 50 g. of fructose.

Much more serious are the four cases described by Froesch *et al.*[3] They were in a 6½-year-old girl, her 2½-year-old brother and two adult males related to the children's father. The parents of these patients were free from this abnormality. The little girl had suffered from frequent bouts of vomiting since infancy, and these were recognized by her mother as being brought on by foods containing sugar. Glucose or dextrin-maltose mixtures failed to produce the vomiting, sweats, tremor and somnolence brought on by fruit, carrots and all sugar-sweetened drinks. Glucose and galactose tolerance tests were within normal limits but the fructose tolerance test was followed by alarming symptoms. There was increasing nausea, sweating, pallor and acrocyanosis followed by vomiting and somnolence which persisted till the next day. The vomitus contained blood. The symptoms gradually cleared after 36 hours. Transient jaundice with elevated serum bilirubin and an abnormal thymol turbidity test, and albuminuria with increased urinary urobilinogen, were present for several days afterwards. Extreme hypoglycæmia (0.008 g. %) was found in the 90-minute sample. It persisted for over six hours and did not begin to return to normal until all the fructose had left the blood; 10% of the ingested fructose was recovered from the urine.

Her brother was apparently not studied but exhibited just as dramatic intolerance to fructose. His mother had learned to avoid fructose in his foods, and his development had been less troublesome. The two adult relatives had been sickly as children and had learned to avoid sugar and fruit, as they used to cause nausea, vomiting and somnolence. This intolerance seemed to have diminished with the years.

Froesch *et al.* postulate an autosomal recessive type of inherited failure of one enzyme system, probably in the liver. Allergy seems to have been satisfactorily excluded as a factor.

The disturbance does not appear to be related to benign fructosuria. It will be interesting to see whether any other cases are discovered, now that these cases have been reported. W. GROBIN

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Medical News in Brief

PROPHYLAXIS AND TREATMENT OF TETANUS

In a recent issue of the *Bulletin of the Johns Hopkins Hospital* (102: 55, 1958) two further papers on prophylaxis and treatment of tetanus are published. The first paper contains experimental work designed to clear up certain disputed points concerning active and passive immunization against tetanus. One disputed point is whether or not tetanus toxoid ought to be simultaneously administered to an injured person together with tetanus antitoxin. The present studies indicate that while the antitoxin response to the toxoid is somewhat suppressed if the dose of antitoxin is simultaneously administered, the effect of the toxoid injection is not altogether lost. This is shown by the fact that a second antigenic stimulus or second dose of toxoid yields a response essentially similar to that in test animals given no antitoxin with their first toxoid injection. These workers also note that in rabbits actively immunized, a high serum antitoxin level affords complete protection even against large challenge doses of tetanus spores, while low serum antitoxin levels are beneficial in that some animals may escape the disease altogether while others have only localized tetanus. Comparable levels of passively transferred antitoxin are much less effective.

Experimental and clinical studies were made of intramuscular and intravenous administration of tetanus antitoxin to patients with tetanus. As a result, it is recommended that a case of tetanus be regarded as a medical emergency and the patient be promptly given a single large dose of tetanus antitoxin by the intravenous route, steps being taken to minimize the chance of anaphylactoid reaction. It is believed that the much more rapid induction of high serum levels of antitoxin by the intravenous route affords therapeutic advantages which outweigh the somewhat greater risk, in all but the mildest cases of tetanus.

CHLORPROMAZINE AND EXPERIMENTAL LIVER CANCER

A preliminary communication about some interesting experiments in cancer inhibition in the Nagoya University School of Medicine, Japan, has appeared in *Nature* (181: 54, 1958). The experiments were conducted to ascertain whether chlorpromazine had any inhibitory effect on the experimental production of liver cancer in rats. Three groups of rats were used, the first receiving the well-known carcinogen, 4-dimethyl-aminoazobenzene, the second receiving the carcinogen plus injections of chlorpromazine, and the third receiving the chlorpromazine without the carcinogen. Whereas most of the 13 rats given the carcinogen for a period of about six months developed hepatic cancer, the group given chlorpromazine as well showed carcinoma of the liver in only one out of the six surviving rats. Moreover, liver cancer production was faster in the group receiving no chlorpromazine, and metastases appeared earlier. This suggests that chlorpromazine has a delaying effect in the formation of experimental liver cancer.

Histologically, noticeable changes were found in the pituitary and adrenals as well as the liver. In the two groups treated with chlorpromazine, atrophy of the pituitary was noticed and there were histological changes both in the anterior pituitary and the adrenals.

TETRACYCLINE AND NYSTATIN IN SKIN INFECTIONS

With a view to establishing the relative efficiency of tetracycline alone and in combination with nystatin, Rein, Lewis and Dick (*Antibiotic Med. & Clin. Therapy*, 4: 771, 1957) treated a series of 350 patients, 90% of whom had pustular acne, in a double-blind fashion, with these drugs. Degrees of therapeutic response based on resolution of pustular lesions were classified according to the observers' judgment of the percentage of improvement of the skin lesions as mild, moderate and marked. Excellent results were obtained with both forms of therapy. Comparable serum concentration levels were obtained whether tetracycline was used alone or in combination with nystatin. It can therefore be implied that nystatin neither enhances nor interferes with the absorption of tetracycline. There was little difference in the over-all incidence of gastrointestinal and other side effects. The authors conclude that the tetracycline-nystatin combination need not be employed routinely where tetracycline therapy is required. However, in debilitated and/or geriatric patients, infants and others in whom monilial superinfection is more likely to occur, the addition of nystatin to tetracycline therapy should seriously be considered, particularly when the latter is indicated for prolonged periods.

ŒSTROGENS FOR MYOCARDIAL INFARCTION IN WOMEN

Marmorston and his colleagues from Los Angeles (*New England J. Med.*, 258: 583, 1958) gave small doses of ethinyl œstradiol orally (10 micrograms daily) to 26 postmenopausal women who had sustained at least one frank myocardial infarction.

No effort was made to restrict fat intake in these patients or to give anticoagulant therapy. In these small doses, the œstrogen had no untoward clinical effects, but it produced a fall in serum cholesterol and a rise in phospholipid levels and a fall in the cholesterol-phospholipid ratio of the same magnitude reported by other investigators using very large doses. The lipid changes were progressive during the first six or seven months of this treatment and by that time the C/P ratio had generally reached a normal level. Further changes upward or downward were not observed thereafter over a period of 30 months. It is noted that the effect of œstrogen on the serum lipids was related to their previous pattern; if this pattern was normal there was little or no effect, but when it was abnormal the change was related quantitatively to the initial abnormality. It is suggested that œstrogens may have a homœostatic effect upon serum lipid levels.

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GENERAL PRACTICE

THE TREATMENT OF CIRRHOSIS OF THE LIVER*

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CIRRHOSIS of the liver, like other chronic diseases for which specific therapy is lacking or unsatisfactory, too often arouses a sense of defeat in the mind of the physician presented with its management. Dr. Duncan Graham once remarked that "It is a too common failing for physicians to dwell upon the imperfections of medical knowledge instead of making the best use of available knowledge." It was with this thought in mind that a review of 50 cases of hepatic cirrhosis, treated at the Victoria General Hospital, Halifax, between 1952 and 1957, was undertaken. Their treatment falls naturally into two parts, that of the underlying disease and that of its main symptoms. If the best use is to be made of such treatment as is available, an effort must be made to determine etiology, and some simple classification, as shown in Table I, is useful.

TABLE I.—CLASSIFICATION OF CIRRHOSIS

I. Portal cirrhosis
  A. Laënnec's cirrhosis
    Diet
    Alcohol
  B. Healed subacute necrosis
    Infectious hepatitis
    Homologous serum hepatitis
    Hepatic poisons
  C. Metabolic cirrhosis
    Hæmochromatosis
      Iron
    Hepatolenticular degeneration
      Copper
      Amino acids

II. Biliary cirrhosis
  A. With extrahepatic obstruction to bile ducts (prolonged)
    (1) Partial
    (2) Intermittent
  B. Without extrahepatic obstruction to the bile ducts.
    (1) Cholangiolytic (Karsner)[1]
    (2) Xanthomatous (Thannhauser)[2]

III. Syphilitic

IV. Congestive

The diagnosis of cirrhosis of the liver is usually not difficult. In Table II, the presenting symptoms of the Halifax patients are shown. All but one of the patients had one or more of the symptoms of jaundice, enlarged liver, hæmorrhage or ascites. The presence of two or more of these symptoms makes the diagnosis relatively easy, as was the case in 31 of the 50 cases reviewed. In the remaining 19, enlargement of the liver alone occurred in 13 cases, ascites alone in 3, and hæmatemesis alone in 2. The diagnosis was unsuspected in the remaining patient, but was made at laparotomy for abdominal pain. In such cases, where only one important symptom or sign is present, some difficulty in diagnosis may be encountered. However, the presence of telangiectases, xanthomata, palmar erythema, pigmentation or abnormal liver function tests usually indicates the diagnosis. Of particular importance and difficulty are the cases of hæmatemesis occurring in the absence of other evidence of liver disease. In such circumstances, the demonstration of œsophageal varices by œsophagoscopy is the most important single diagnostic procedure.

TABLE II.—CIRRHOSIS OF THE LIVER, VICTORIA GENERAL HOSPITAL, HALIFAX, N.S., 50 CASES, 1952-1957

Presenting symptom or sign	*No.*	*%*
Jaundice	19	38
Large liver	10	20
Hæmorrhage	7	14
Ascites	5	10
Anorexia	4	8
Other	5	10

The treatment of the underlying disease demands a knowledge of the type of cirrhosis to be treated. The distribution of the various types found in the Halifax series as shown in Table III indicates that portal cirrhosis is by far the commonest type encountered. In Table IV are shown the recognized factors which play a part in the production of cirrhosis. Alcohol and poor dietary intake were considered important in 12 of the 40 patients with portal cirrhosis. The studies of Best[3-5] and his coworkers have led to the firm knowledge that diets deficient in choline and its precursors render the liver more susceptible to hepatotoxins and cause the deposition of fat in the liver, with subsequent cirrhosis. Therefore, a diet high in protein, a source of choline, is clearly indicated. If such a diet is taken by the patient, it is doubtful whether the addition of supplements of choline or its immediate precursors adds significantly to the treatment. Similarly, it has long been known that a liver rich in glycogen withstands hepatotoxins better than a liver which has been depleted of glycogen by starvation. It is, therefore, reasonable to feed a diet high in carbohydrate. Too often, a low fat

TABLE III.

Type of cirrhosis	
Portal	40
Obstruction	6
Non-obstructive biliary	2
Hæmochromatosis	1
Hepatolenticular degeneration	1

TABLE IV.

Known underlying causes
Diet
Alcohol
Iron
Copper
Hepatotoxins
Syphilis
Congestion
Extrahepatic obstruction

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diet is ordered. There is no evidence that a reasonable amount of fat is harmful. The prescription of a low fat diet does not indicate clearly the desirable features of high protein and high carbohydrate, and severe restriction of fat produces an unpalatable diet.

The role of alcohol in the production of cirrhosis has been much debated over the years. Varying figures for the incidence of unusual alcohol consumption in cirrhotics have been reported before and since Matthew Bailey's writings in 1793. Often, as in the Halifax series, such alcoholic intake was associated with poor diet. On the other hand, many redoubtable drinkers have lived their life span without the development of cirrhosis, and many people have developed cirrhosis who have never taken alcohol in their lives. Cirrhosis is common in certain races whose diet is deficient in protein, and who do not use alcohol. Cirrhosis has never been produced in animals by the administration of alcohol. However, the production of cirrhosis in rats by diets deficient in choline is enhanced by the simultaneous administration of alcohol.[6] The evidence indicates the complete exclusion of alcohol from the diet of the cirrhotic patient.

Hæmochromatosis is considered due to unusual absorption of iron from the intestine with the result that iron stores are built up to higher than normal levels and iron is deposited in some cells far in excess of normal amounts. The principal organs affected by such deposition are the liver, pancreas, and skin. Treatment by the repeated withdrawal of blood to reduce iron stores by increasing the requirements for blood formation has been recommended. As yet, experience is insufficient to permit judgment as to its efficacy.

The exact significance of the high copper content of the liver and the high excretion of copper and amino acids in the urine of patients with hepatolenticular degeneration (Kinnear Wilson's disease) has not been elucidated as yet. Nevertheless, a distinct improvement in the neurological manifestations of the disease has been observed following the administration of BAL (British Antilewisite). It is to be hoped that similar benefit to the liver may result, but again, evidence of this is lacking.

Healed subacute necrosis of the liver resulting from recognized hepatotoxins is rare. Complete recovery from infectious hepatitis or homologous serum jaundice occurs in the very great majority of the cases. Nevertheless, the work of Sherlock leaves no doubt that in a very small percentage of the cases, such hepatitis occurring in a liver previously normal may progress through a stage of damage to stroma and blood vessels, to healing with scar, and eventual death from hæmatemesis. This is a reason for considering infectious hepatitis a potentially dangerous disease, and treating it with adequate rest and dietary measures.

The effective treatment of syphilis has made healed gumma of the liver rare. Even when it does occur, it seldom produces alteration in hepatic function. Nevertheless, any patient with hepar lobatum should receive a course of penicillin to eliminate any living spirochætes which may remain.

Congestive cirrhosis is a controversial subject. If the livers of patients who have had prolonged or repeated bouts of congestive heart failure are examined, nearly all will show increase in fibrous tissue diffusely throughout the organ. Such change usually causes no symptoms. Only about 5% of this particular group of cases have cirrhosis of sufficient degree to cause any disorder of function and so simulate Laënnec's cirrhosis. Such a very low incidence leads to the question whether the patient has portal cirrhosis as an additional finding to congestive heart failure, or whether the cirrhosis is truly the result of the hepatic congestion. It makes very little difference in practice, as the patient's treatment is primarily that of congestive failure and it is likely that the patient will die of heart disease before any significant trouble from cirrhosis. In the Halifax series, there were no cases considered to be due to congestion.

Prolonged, incomplete or intermittent obstruction of the common bile duct results in cirrhosis of the biliary type. The relief of such an obstruction is indicated, but its beneficial effect on the cirrhosis will depend in part on the duration of the obstructing lesion, and consequently the degree of damage which the liver has sustained. The usual obstructing lesions are stone, stricture or neoplasm. In the case of neoplasm, it is usual for the patient to die of the disease before significant cirrhosis develops, but in some instances of slow growing tumours, a well-marked cirrhosis occurs. When such a tumour is situated in the region of the porta hepatis, its recognition may be difficult even at operation. Such cases can easily be confused with non-obstructive biliary cirrhosis, as pointed out by Dauphinée.[7]

The symptomatic treatment of cirrhosis of the liver has become increasingly complex in recent years. The incidence of the chief symptoms of the disease, as they occurred in the Halifax series, is shown in Table V.

TABLE V.

Incidence of chief symptoms and signs	*Cases*	*%*
Jaundice	23	46
Ascites	13	26
Hæmorrhage	8	16
Anæmia	21	42

The treatment of jaundice is dependent upon the treatment of the underlying disease; for the itching with which it may be associated, no effective treatment is known.

Ascites resulting from cirrhosis of the liver is due to varying combinations of damage to capillaries, lowered osmotic pressure of the blood due to decreased amounts of serum albumin, and increased hydrostatic pressure in the portal system associated with portal hypertension. To these primary factors is added increased excretion of aldosterone[7] and possibly also of pituitary antidiuretic hormone with resultant retention of water and salt. It would be of interest to know the relationship of aldosterone level, antidiuretic hormone level and portal venous pressure to episodes of ascites occurring at various stages of liver disease. It is difficult to believe that

the ascites occurring in acute liver disease with normal serum protein levels has the same cause as that in far advanced cirrhosis with depleted serum albumin. Nor does it seem likely that either comes about in the same way as do the episodes of ascites preceded by acute abdominal pain of unknown cause or the ascites that may occur in patients with a large fatty liver whose enlargement disappears when adequate dietary therapy is instituted. The observation that reduction of portal hypertension by shunt operations is seldom beneficial to the course of ascites does not necessarily mean that portal hypertension does not play a part in its development. In many cases, the institution of a low sodium diet and the exhibition of mercurial diuretics prove effective in counteracting the retention of water and salt and decreasing the accumulation of ascitic fluid. This is to be preferred to repeated abdominal paracenteses since these deplete the plasma protein.

The treatment of hæmorrhage constitutes one of the most difficult problems in the management of cirrhosis. The immediate management of the case consists in the treatment of shock by the transfusion of whole blood, and attempts to arrest the bleeding by the insertion of a tube connected to a hydrostatic bag which can be distended in the lower œsophagus. Once the emergency is over, some thought must be given to more definitive treatment. In the majority of cases, the presence of ascites or jaundice, or the onset of hepatic coma following the hæmorrhage, will clearly indicate that no such efforts should be undertaken. Occasionally, however, repeated episodes of hæmorrhage may be the only manifestation of liver disease for many years, and in such cases, benefit can result from a procedure which will reduce the pressure in the portal system. It is in this small group of cases that shunt operations have their greatest value. Such operations are difficult technically, and are contraindicated by jaundice, ascites or a bromsulphalein retention above 15% at 45 minutes, because of the danger of hepatic coma. Exact indications for and contraindications to this operation have not as yet been satisfactorily delineated. However, it is fair to say that the more the indications are broadened, from the ideal group described above, the greater the risk becomes. At best, it is an operation which in expert hands will be beneficial to a small group of patients.

TABLE VI.

Types of anæmia	
Acute blood loss	8
Chronic blood loss (iron stores depleted)	6
Hypersplenism (pancytopenia)	3
Macrocytic	2
Normocytic normochromic	2

In Table VI are shown the types of anæmia encountered in the Halifax series. Anæmia of acute blood loss will recover just as rapidly without the administration of iron as with it. Transfusion is indicated for shock, rather than for the anæmia. The anæmia of chronic blood loss with depleted iron stores requires the administration of iron by mouth, and in the very rare cases in which oral iron is not tolerated parenteral iron is indicated.

Pancytopenia due to hypersplenism occurred in three cases in this series. In two, the anæmia was readily controlled by periodic transfusion of whole blood. In the third, it constituted a major problem, and consideration of the patient's case history is of interest:

> The patient, a man aged 60, first came under observation at the age of 57, in 1954, suffering from portal cirrhosis thought to be due to dietary deficiency and excessive consumption of alcohol. It gave rise to jaundice, ascites, hepato-splenomegaly and anæmia. The anæmia was normocytic and normochromic. The white cells and platelets were depleted. The bone marrow was hyperplastic. There was no evidence of bleeding. On a good dietary regimen and the withdrawal of alcohol, the patient's underlying disease improved to the extent that jaundice and ascites cleared, and he remained well for the next three years, except for the persistence of anæmia which required periodic transfusion of whole blood. Between July 1955 and July 1956, the patient was transfused every three months with amounts varying between 1500 and 2000 c.c. each time. For this reason, the patient was subjected to splenectomy in July 1956. At the same time, a splenic-renal shunt was done because of the presence of large œsophageal varices which had been demonstrated both by x-ray and œsophagoscopy. Since that time, the patient has not required transfusion. An examination of his blood in May 1957 revealed a platelet count of 300,000 and a blood film which appeared normal apart from slight macrocytosis.

While this patient, in all likelihood, will eventually die of hepatic failure, his health has been greatly improved and he has been able to enjoy an active life.

Many patients with cirrhosis show a mild degree of rather generalized macrocytosis. In a few patients—two in this series—the macrocytosis is marked and may lead to confusion in diagnosis with Addisonian pernicious anæmia. It differs from the latter in that the cells appear thin, reticulocytes in the circulating blood are increased, and the bone marrow is not megaloblastic. Some observers have felt that large doses of liver extract benefit this anæmia. It is the experience of others, including the author, that liver extract, vitamin B_{12}, and folic acid are of no value in the treatment of this anæmia, but that it does tend to improve if general measures result in improvement of the underlying disease.

Hepatic coma has been the subject of rather intensive study for the last few years, particularly in relation to the accumulation of ammonia in abnormal amounts in the blood. It has been shown that the administration of ammonia to dogs will produce neurological symptoms similar to those seen in hepatic coma. In human beings with hepatic coma, the blood ammonia has been found to be elevated. Such elevation can be reduced by the administration of broad-spectrum antibiotics which reduce the production of ammonia in the gut, or by the administration of arginine or sodium glutamate which facilitate its metabolism. However, the cor-

relation of hepatic coma with the level of blood ammonia has not been very satisfactory, and treatment directed at the lowering of blood ammonia would not appear to have significantly altered the expected course of the disease. Furthermore, such treatment usually has been associated with the administration of fluid, glucose and various electrolytes, and it is difficult to separate one effect from another. At the present time, it must be considered that the role of ammonia in hepatic coma has not been entirely clarified. Patients who have had an episode of hepatic coma or who have impending hepatic coma are said to benefit from restriction of protein in their diet as another measure for the reduction of blood ammonia. In most cases, where hepatic coma is present or threatened, little benefit is to be expected from a high protein diet in any case, and it is only wise that a diet restricted in protein be given.

SUMMARY

Fifty cases of cirrhosis of the liver, treated at the Victoria General Hospital, Halifax, in the period of 1952 to 1957, are reviewed and certain significant findings presented to form a basis for the discussion of the treatment of this serious disease. The treatment of the known underlying factors influencing the development of the disease has been considered and the management of the major symptoms of the disease considered in detail. In conclusion, it may be said that while much is lacking in our knowledge of the pathogenesis and treatment of the underlying disease, utilization of this knowledge can bring great relief to many patients suffering from cirrhosis.

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GENERAL PRACTICE RESIDENCIES

THE COLLEGE OF GENERAL Practice of Canada brings to the attention of those about to graduate, and of recent graduates, their Residency Training Program.

This residency training is designed for the young physician who is desirous of making a career in general practice. The program is designed to be more meaningful than simply a second year of rotating internship. While a second year of training is in itself a desirable educational experience, the College of General Practice feels that its Residency Training Program offers even more. It is an attempt to acquaint the resident more specifically with some of the problems, realistically, which he must face, as well as to afford the opportunity for a greater breadth and depth of medical knowledge.

Residency Training Programs have been established at the following hospitals:

Alberta:

Holy Cross Hospital, Calgary, Alta.; Sister C. Gauthier, Superior and Administrator.
Misericordia Hospital, 9830-111th Street, Edmonton; Dr. A. J. Brunet, Medical Director.
St. Michael's General Hospital, 13th St. & 9th Ave. S., Lethbridge; Sister M. Consolata, Administrator.

British Columbia:

Royal Jubilee Hospital, Victoria; Dr. J. L. Murray Anderson, Medical Administrator.
St. Joseph's Hospital, Victoria; Dr. E. N. Boettcher, Medical Superintendent.

Manitoba:

St. Boniface Hospital, St. Boniface; Dr. Paul L'Heureux, Medical Director.
Misericordia General Hospital, Winnipeg; Dr. Jack McKenty, Secretary of Executive Staff.
Victoria Hospital, Winnipeg; Dr. G. B. Rosenfield, Administrator.

New Brunswick:

Saint John General Hospital, Saint John; Dr. Carl R. Trask, Director.

Nova Scotia:

Aberdeen Hospital Commission, New Glasgow; Dr. H. C. McKay, Medical Superintendent.

Ontario:

Belleville General Hospital, Belleville; Mr. Kenneth E. Box, Administrator.
Hôtel-Dieu Hospital, Cornwall; Sister St. M. Magdalen, Administrator.
Ottawa General Hospital, Bruyère Street, Ottawa; Dr. J. Paul Laplante, Medical Director.
The General Hospital of Port Arthur, Port Arthur; Mr. J. A. McNab, Administrator.
St. Thomas-Elgin General Hospital, St. Thomas; Mr. Bertram G. Thacker, Administrator.
St. Joseph's Hospital, Sarnia; Sister M. St. Paul, Superintendent.
New Mount Sinai Hospital, 550 University Avenue, Toronto; Mr. Sydney Liswood, Administrator.
Northwestern General Hospital, Keele St., Toronto 9; Dr. V. C. Malowney, Chief of Staff.
St. Joseph's Hospital, Toronto; Sister M. Estelle, Superintendent.
Toronto East General and Orthopædic Hospital, Coxwell at Sammon Ave., Toronto 6; Mr. E. R. Willcocks, Superintendent.

Quebec:

Montreal General Hospital, Montreal; Dr. William Storrar, Medical Director.
Notre-Dame Hospital, Montreal 24; Dr. J. R. Boutin, Medical Director.
Royal Victoria Hospital, Montreal 2; Dr. Ronald V. Christie, Physician-in-Chief.
Hôtel-Dieu de Québec, Québec; Dr. J.-B. Jobin, Medical Director.
Hôpital St-Joseph, 779 Ste-Julie, Trois-Rivières; Dr. J. J. Laurier, Medical Director.

Saskatchewan:

Regina General Hospital, Regina; Dr. H. E. Appleyard, Superintendent.
St. Paul's Hospital, Saskatoon; Sister A. Lachance, Administrator.

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MISCELLANY

FATHER WAS A MEDICINE ADDICT

GEORGINA H. THOMSON, *Calgary, Alta.*

Father was what one might call a medicine "addict". Mother used to tell how, when they were married and moved into their first home, they found a whole shelf of bottles and boxes of medicine left by the previous tenant. Father was delighted and, before he was through, took the whole thing, on the general principle that medicine *per se* was "good for you". All his life he was a firm believer in the efficacy of medicine, and never thought a doctor was doing anything for him unless he prescribed generous quantities of pills, powders and syrups.

If Father had lived in the day of TV's seductive advertisements one might have understood the fascination, but perhaps the media of his own day had their own appeal. There in the backwoods of Ontario a smooth-talking pedlar, asked to stay for supper and spend the night, could get in some pretty good "plugs" for the pain-killers, salves and cough mixtures he carried. One could picture Father too as a young lad in town for the excitement of the district fair, listening spellbound to some medicine-man, perhaps in Indian headdress and regalia, holding forth on his nostrums and elixirs.

However it came about, he was certainly indoctrinated. Not that he had ever been a puny, sickly person. True, he used to tell us that he never went to school much because he was delicate, but when we tried to pin him down to his precise ailments, he would grin and finally admit, "I guess I just didn't like school." He was quite capable of putting on a very convincing act for Grandma's benefit till after the school bell had rung and he might safely leave his bed. Yet he himself used to brag about his youthful prowess as a wrestler and weight-lifter, and how he ploughed with a walking plough and a team of oxen when he was a mere child. We always suspected these tales to be slightly embroidered, as the age of the ploughman became progressively younger as time went on.

The fact remains, however, that Father must have had a tremendous vitality, for he lived to be 95 and never spent a day in hospital. Whether this was due to, or in spite of, the medicine he took is anybody's guess. We know what he would have said. He had absolute faith in the efficacy of the various cures he took. He used to tell us how once when he had what was then called "inflammation of the eyes", on someone's recommendation he put a patent pain-killer undiluted into his eyes. In agony from the searing burn, he plunged his face into cold water. "But it cured me," he said, and he would never admit in later years that this might have been the original cause of his loss of sight. He was over 80 by then and of course may have been right when he said it was due to his age alone.

Father had an especial fondness for pills. As far back as I can remember, his standard excuse for not going to church was that he had taken a pill. We used to think that this was just a way out for him, but the fact remained that he usually *had* taken a pill.

Almost always Father had some sort of pill that he took before his meals, and we must always have the bottle beside his plate. In those last hectic moments that always come when one is trying to assemble a dinner and get the roast, the gravy, vegetables and hot plates to the table simultaneously, we would hear Father call, "Where are my vitamin pills?" That to him was the most important item of the meal.

After our mother's death, my sister and I sometimes hid certain pills or medicines that we thought were harmful to him, but he was always quite indignant. "*I* know what's good for me," he would say. Occasionally in a reckless mood we would throw out the offending pills, only to have to go to the drug-store and get more at his demand. After all, when his mother, his six sisters and then our own mother had given in to him all those years, what chance had we when he was in his eighties?

I should not like to give the impression that Father was a gloomy old hypochondriac. He may have been a tyrant but he was a very cheerful, affectionate tyrant, and grateful for anything we did for him. He would say, "If I were a millionaire, I could not be better looked after." He never admitted that he was old, or talked of dying. He never complained about his very real affliction, loss of sight, and if he failed to recognize friends when they dropped in, he would bluff it out till we were able to drop him a casual hint as to who the visitors were. He was plucky and independent in other ways, such as refusing to have his meals in bed. Scrubbed and immaculate, he preferred to come to the table "on his own steam" if he possibly could.

It was just that taking medicine was a mild sort of dissipation for him, and I don't think he ever opened a box of pills without a little thrill of pleasure. One of his favourites was a certain well-advertised brand of kidney pills. He always said they helped his back, though we could never see that there was much wrong with his back. One day when he opened a box of them, the lid stuck and finally came off with a jerk, causing one or two of the pills to fall out on the floor and roll away under the couch. Father's sight was so poor that although he got down on his knees, he could not at first locate the missing pellets, so he lit a match and waved it back and forth under the couch till he found them. Putting them back into the box, he walked out of the room and forgot all about the incident. Later, when my sister came down stairs, she was horrified to find the living-room full of smoke, and see flames leaping out from the couch.

When the fire-brigade had been and gone and the living-room rugs and furniture were dismally wet and smoke-begrimed, Father remembered about the match and confessed. Next day the regular advertisement for these pills came over the radio, ending with its slogan "Easy to take". "But hard to find," added our Irish brother-in-law. Father received the remark in stony silence.

All radio advertisements for patent medicines interested Father intensely, and he believed every word of the honey-toned announcers. "They say Blank's Cough-mixture is very good," he would say. We would try to explain that *they* were just radio announcers reading advertisements paid for by the manufacturers of the product. He would remain convinced of the virtues of the nostrum extolled so unctuously by the radio voice, and taking some change out of his pocket would say, "Well, get me some anyway when you are over at the store. I'd like to try it."

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As Father grew older and some of the aches and pains of old age began to catch up with him, he redoubled his efforts to find cures. Getting him to bed involved quite a ritual. He had a pathetic confidence that all would be well if he could only find the right medicine. The rattle of pills would come from his room as he doled out his self-prescribed number with all the seriousness of a professional pharmacist—digestive pills, aspirin, and always cathartics, for like many old people he became preoccupied with his bowels. His general good health was the triumph of a strong constitution over persistent indulgence in strong palliatives.

He always had to have a glass of sodium bicarbonate and water beside his bed, and though we had mixed it for him a thousand times, he always gave us exact instructions—half a teaspoon of soda in three-quarters of a glass of *cold* water. "Let the tap run a while," he would say. For a time he took a raw egg in a glass every night, and usually two tablespoons of mineral oil.

In later years he kept a small bottle of whisky under his pillow in case he felt a little weak in the night. My sister used to dilute it for him, and one night when the supply was running rather low, she drew a little more than usual from the tap. In the middle of the night, we heard an outraged cry from his room—"It's been watered!"

Every night Father applied various salves and ointments to different parts of his anatomy—a callous on his rear, an itchy place on his ankle, a rough place on his cheek. Then there were drops to be put in his eyes, alcohol to be rubbed on his legs, and the current cough-mixture to be administered. Finally, when he could think of nothing further, we adjusted his pillow to his liking, tucked the covers around him and kissed him good-night.

As Father neared his 95th birthday, he seemed to have an inner foreboding that all was not well with him, in spite of all the concoctions he had swallowed through the years. "I would take *anything*," he said sadly, "if it would only bring back my strength." Then a happy thought struck him. "Go over to the drugstore and asked Charlie to recommend something. He fills out a lot of prescriptions for the doctors and he must know of something that will help." (No matter how kind and attentive the family doctor was, Father always felt that he was a little bit sticky about ordering medicine.)

We went over and consulted Charlie, who sent over some harmless thing, but Father didn't take it after all. The next morning something snapped in the old mechanism and Father went to sleep without pain in his own familiar room, with his daughters keeping watch beside his bed.

Afterwards we gathered up all the boxes of pills and bottles of medicine and jars of salve from his dresser and put them away with a smile of tender indulgence. The drugstore had lost a good customer, but after all, who were we to say that Father did not know what was "good for him"?

3012 5A St. S.W.,
Calgary, Alta.

Association Notes

COMMITTEE ON ECONOMICS

The Committee on Economics of the Canadian Medical Association met in Toronto on March 7 and 8, with Dr. R. K. Thomson of Edmonton in the chair. Dr. E. Rolland Blais, Montreal; Dr. Richard Thérrien, Quebec; and Dr. Jean Térrien, Ottawa, represented l'Association des Médecins de Langue Française du Canada.

Dr. Kelly reviewed the situation concerning the use of provincial fee schedules by the Department of Veterans Affairs. (This has already been mentioned in the report of the last meeting of the C.M.A. Executive Committee.) The Committee was also told that the officials administering the medical services for sick mariners will use the same arrangement, namely, payment at the 90% level of provincial fee schedules. Furthermore, the Department of National Defence has started to use this method of payment where members of the Armed Forces are treated by private physicians. After some discussion, it was emphasized once more that payment at the 90% rate was accepted under protest; if experience was satisfactory, it might be possible to obtain payment of 100% of the schedule at some future date.

Mr. Freamo, Assistant Secretary, C.M.A., presented an interim report on relative value studies, listing 12 factors to be used as the basis for evaluating opinions and procedures in medical practice. The Committee discussed these factors and made comments to assist in the future development of the study. After further discussion of proposed steps for the continuation of the study, it was agreed that each divisional chairman of the Committee on Economics should set up a plan by which physicians in each division might be selected who were capable of analyzing medical opinions and procedures in terms of their relative value.

After a full discussion of the new Children's Health Service in Newfoundland, the Committee turned its attention to the question of arbitration and negotiation between members of the medical profession and other organizations. It had been asked to study this question by the Executive Committee and it finally recommended that the following statement be inserted after paragraph 19 in the Statement of Policies and Principles on Health Insurance in Canada:

"It is essential that any member or group of members of the medical profession have the same fundamental rights as other citizens to choose the type and location of practice and to negotiate agreements covering methods of remuneration, conditions of providing professional services and modification or termination of contracts."

To implement this statement the Committee recommends:

"1. That all members of the profession and governments recognize the Canadian Medical Association and its divisions with l'Association des Médecins de Langue Française du Canada, when indicated, as the negotiating body of the medical profession.

"2. That the position of the profession be strengthened by measures designed to unify the profession and to gain greater support from the public.

"3. That the importance be recognized of adequate contractual arrangements and that informative documents be prepared delineating acceptable standards of contracts and methods of negotiation."

The Committee was advised that the Industrial Disputes Investigation Act, under which employees may be represented by unions for purposes of collective bargaining, is being reopened. Under existing legislation, professional persons such as physicans may not be represented by a union for collective bargaining. The Committee reaffirmed the view that organized medicine rather than unions should assume the responsibility for improving the position of all doctors, including those on salary, and felt that there was no indication that physicians should be active members of a union.

The Committee discussed present negotiations between the divisions of the C.M.A. and governments with respect to the administration of physicians' services contemplated under Bill 320. It recommended (1) that the services of the C.M.A. be made available on request to any division negotiating with Government; (2) that in provincial hospitalization programs, the principle be re-endorsed of administration by a commission representative of those persons providing and receiving the service; (3) that wherever medical services are provided to persons whose medical care is the responsibility of Government or other third parties, the professional component of this care be compensated for separately and in accord with an agreement based on fee for service; (4) that the responsibilities of the profession in health insurance relative to the maintenance of standards of care and control of abuses are best fulfilled by professional representation on provincial and local committees advisory to the health insurance authorities.

There was further discussion of the question of uniform insurance forms. The Committee authorized Dr. Lang and Dr. Peart to proceed with the setting up of a form which might be used as a basis for discussion with the insurance companies.

A report on the proposed T.C.M.P. National Underwriting Agency was received, but it was agreed that Committee members should be given the opportunity to discuss the report in their own divisions and with local plans and report back at a subsequent meeting.

TRAVELLING TO GREAT BRITAIN IN 1958?

Canadian doctors proceeding to the United Kingdom this summer can materially assist their British colleagues who have plans to visit Canada.

An official B.M.A.-C.M.A. currency exchange plan will help three doctors from the United Kingdom to obtain dollars for their expenses in Canada. Here is how it works. Three British doctors deposit £200 with the B.M.A. and receive $540 on arrival in this country. Balancing the transaction, we collect $540 from three Canadian doctors and the B.M.A. provides them £200 when they arrive in Britain.

If you desire to participate in this excellent arrangement at any time during 1958, send in your cheque for $540 made out to The Canadian Medical Association, giving the date and method of travel. The B.M.A. will provide the sterling currency at any point which you designate. You are invited to communicate with the General Secretary, C.M.A., 150 St. George Street, Toronto 5.

RAIL TRAVEL TO HALIFAX

Low convention fares to Halifax are available; for example, the fare from Toronto to Halifax and return is $74.65, and parlour car chairs between Toronto and Montreal are $2.55 each way. The following rates apply to sleeping car accommodation between Montreal and Halifax:

MONTREAL—HALIFAX (EACH WAY)

Lower Berth	*Duplex Roomette*	*Bedroom*		*Compartment*		*Drawing Room*	
		(1)	*(2)*	*(1)*	*(2)*	*(1)*	*(2)*
$6.85	$8.25	$13.70	$15.45	$17.50	$19.50	$21.00	$24.00

TRAIN SERVICE, FROM TORONTO (EASTERN STANDARD TIME)

Going				
Leave	Toronto	9.15 a.m. 1st day	or	11.30 p.m. 1st day
Arrive	Montreal	4.20 p.m. 1st day		7.30 a.m. 2nd day
Leave	Montreal	8.30 p.m. 1st day		10.30 a.m. 2nd day
Arrive	Halifax	5.45 p.m. 2nd day		1.20 p.m. 3rd day
Return				
Leave	Halifax	11.45 a.m. 1st day	or	6.45 p.m. 1st day
Arrive	Montreal	7.50 a.m. 2nd day		6.55 p.m. 2nd day
Leave	Montreal	8.20 a.m. 2nd day		11.00 p.m. 2nd day
Arrive	Toronto	3.15 p.m. 2nd day		7.15 a.m. 3rd day

For reservations or further information, contact Mr. R. H. Scott, Canadian National Railways, 55 Yonge Street, Toronto, or phone EM. 6-9011, Local 461. *Reservations should be made at the earliest possible date.*

MEDICAL SOCIETIES

CANADIAN ANÆSTHETISTS' SOCIETY

The following items appear on the program of the annual meeting of the Canadian Anæsthetists' Society, which will be held at the Seigniory Club, Montebello, Que., on June 23, 24 and 25.

Monday afternoon: Dr. J. Gordon Robson—"Some Observations on Regurgitation and Vomiting During Anæsthesia"; Dr. F. A. Walton—"Promethazine with Anæsthesia"; Dr. Allen B. Dobkin—"The Effect of Anticholinergic Drugs on the Cardiac Vagus"; Dr. R. A. Millar—"Studies with Hæmorrhagic Hypotension".

Tuesday morning: Dr. Eva M. Kavan—"EEG and ECG Patterns During Intracardiac Surgery Using the Cardiopulmonary Bypass—A Comparison of the Effect of Different Anæsthetic Agents"; Dr. D. LeRoy Crandell—"The Role of the Anæsthesiologist in the Management of Severe Systemic Tetanus".

Tuesday afternoon: Dr. Fernando Hudon and Dr. André Jacques—"Fluothane-Ether Mixture"; Dr. I. M. MacKay—"A Clinical and Laboratory Evaluation of Four Fluothane Vaporizers"; Dr. Gordon M. Wyant—

"Serial Cardiac Output Determinations during Fluothane Anæsthesia"; Dr. R. G. B. Gilbert—"Second Thoughts on Fluothane in Neurosurgery".

Wednesday morning: Dr. Eric Webb—"Ten Years of Group Practice"; Dr. M. Keeri-Szanto and Dr. J. Labarre—"Serum Protein Changes in Thiopental–Nitrous Oxide Anæsthesia"; Dr. H. B. Graves—"Shock in Obstetrics"; Dr. J. Rosales and Dr. T. Davenport—"Difficult Endotracheal Intubation of Infants and Children".

Wednesday afternoon: *Reports of Work in Progress*—Dr. R. G. B. Gilbert—"Preliminary Studies with a New Short-acting Intravenous Anæsthetic Agent"; Dr. J. Beldavs—"Intramuscular Relaxant in Infants"; Dr. G. Fortin and Dr. W. Tremblay—"The Short-Needle Technique in Brachial Plexus Block"; Dr. L. Lamoureux and Dr. J. Lafleur—"The Pudendal Block Technique for Both Sexes: Value, Advantages and Disadvantages"; Dr. Marjorie Bennett—"Preliminary Report on the Use of G-29505"; Dr. J. J. Carroll—"The Anti-hypnotic Effect of Ritalin"; Dr. S. M. Campbell—"Evaluation of Pipadone"; Dr. Ian Purkis—"The Potentiation of Obstetrical Analgesia by Tranquillizers"; Dr. R. A. Miller—"Plasma Catechol Amine Levels"; Dr. G. I. McGillvray—"Comparative Study of Histamine Release by Various Opiates"; Dr. T. Davenport—"Investigation of Cardiovascular Effects of Fluothane"; Dr. Rosario Denis—"Preliminary Study on the Problem of Alkalosis in Anæsthesia".

The annual general meeting will take place at 10.30 a.m. on Tuesday, June 24, and the dinner of the Society at 7 p.m. on that day.

CANADIAN CANCER SOCIETY

TAKE NOTICE that the 1958 Annual Meeting of the Canadian Cancer Society will be held in the Isle Royal Hotel, Sydney, Nova Scotia, Monday, June 9, at 11:00 a.m. (local time) to receive the reports of the Directors and the Auditors and to transact such other business as may properly be brought before the meeting.

By Order of the Directors,
GEORGE PIFHER,
Secretary-Treasurer.

PUBLIC HEALTH

COMMUNICABLE DISEASES IN CANADA

DURING THE WEEK ending March 29, 1958, the Epidemiology Division of the Department of National Health and Welfare, Ottawa, received the following reports of communicable diseases.

SCARLET FEVER

Annapolis County, N.S.—Dr. G. M. Smith, Medical Officer of Health, Fundy Bay, reports 30 cases of scarlet fever, apparently mild. Whole families are affected. There are many other cases that are not seen by physicians.

Bowness-Montgomery, Alta.—Dr. D. N. Keys, Medical Officer of Health of the Mount View Health Unit, advises that a considerable number of cases of scarlet fever and septic sore throat have been reported by physicians.

DIPHTHERIA

Valleyview and Crooked Creek, Alta.— Dr. P. P. Rowan, Medical Officer of Health of the Grande Prairie Health Unit, reports a diphtheria outbreak at Valleyview. Altogether there were three cases and two carriers: two confirmed cases in fully immunized children; one clinical case in an adult, not confirmed bacteriologically, and one carrier aged six years. The first child affected is a sister of the carrier and the other child who developed the disease is a classmate. The adult case was not in contact with the other cases or the carrier.

Cow-Pox

Wanham, Alta.—A case of cow-pox contracted from an infected cow occurred at Heart Valley. The patient had three pustules, two on fingers and one on the forehead.

INFLUENZA

INDIAN AND NORTHERN HEALTH SERVICES.—The following reports have been received from Dr. P. E. Moore, Director, Indian and Northern Health Services, and Dr. J. S. Willis of the Northern Health Services.

Contwoyto Lake, Alta.—Dr. W. L. Falconer, Regional Superintendent, Foothills Region, reports that following an outbreak of influenza affecting 21 persons, six patients suffering from pneumonia were evacuated to the Yellowknife Municipal Hospital. One died on the night of admission.

Resolute Bay, Alta.—An outbreak of influenza struck all the Eskimos living in this settlement. One of the Eskimos who went to Churchill, Manitoba, to have his eyes examined, fell ill on his return. The disease soon spread to all the other Eskimos living there. There was one death, in a seven-month-old baby, from pneumonia. The epidemic has subsided and all the Eskimos are now in good health.

Fort Providence, Alta.—During March there was an epidemic of influenza at Fort Providence, N.W.T. The Residential School has been closed and there were 90 cases at the Mission School. In addition 50 cases occurred in the village, including whites. The epidemic is now under control.

Hay Lakes, Alta.—Fifty-four children at the school at Habay had influenza-like symptoms, consisting of low-grade pyrexia and severe headaches. All these children had influenza last fall.

DIPHTHERIA

Saddle Lake Agency, Alta.—Two cases of diphtheria have occurred in this settlement, affecting a girl five years old and her baby brother. Both were fully immunized, having had three inoculations of D.P.T.

DYSENTERY

Key Reservation, Fort Qu'Appelle Zone, Sask.—Dr. A. B. Jones, Norquay, reports a proven case by culture of infection by *Shigella flexnerii* in Norquay Hospital and another suspect in Kamsack Hospital. Other cases are occurring on the reservation. Specimens have been sent to Fort Qu'Appelle Indian Hospital. There are about 214 residents on the reservation.

LETTERS TO THE EDITOR

SUBUNGUAL HÆMATOMA

To the Editor:

A few months ago a rather complicated device was shown in your journal (77: 603, 1957) for treating the common condition known as subungual hæmatoma. A much more widely applicable method was once demonstrated to me and I have found it quite effective.

Take an ordinary paper clip and bend out the wire to form a small handle. Then heat the tip of the wire over a flame until it is red hot and apply it over the blood clot, thus burning a hole through the nail. The process is rapid, although several heatings of the wire are needed, and the result is perfect, for the hole is large enough to ensure adequate drainage and yet will not prematurely seal over.

The method is painless (unless injudicious pressure forces the wire into the underlying nail bed) but the odour and patient observation often will produce fainting unless the patient is told to lie down while the procedure is carried out.

ROBERT J. WHITTY, M.D.

Suite 303,
1590 Ouellette Ave.,
Windsor, Ontario,
March 24, 1958.

TREATMENT OF SCHIZOPHRENIA

To the Editor:

I hope that I may be allowed to comment on some points mentioned by Dr. D. E. Cameron and Dr. S. K. Pande in their paper "Treatment of the Chronic Paranoid Schizophrenic Patient" (*Canad. M. A. J.*, 78: 92, 1958).

To get the best results, regressive shock treatment should be continued until the patient is so confused that he does not respond to his name and is doubly incontinent. In other words the patient is regressed to infant levels.[1, 2] Occasionally a paranoid patient cannot be regressed, even after receiving E.C.T. four times daily for a month or more.[3]

The authors state that 100% of the patients treated by regressive shock plus continuous sleep treatment improved enough to be able to leave the hospital. From these figures it can only be assumed that patients with an unfavourable prognosis were excluded from this study and that therefore these results cannot be expected in the general mental hospital population.

M. G. JACOBY, M.B., B.S.

Central Islip State Hospital,
Central Islip, N.Y.,
March 15, 1958.

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THE PARABLE OF EACH AND ALL

To the Editor:

Once upon a time, in a far away land, there was a beautiful country where the songs of the birds were sweeter, the sun shone more brightly, the flowers bloomed more abundantly and the wind and the water whispered together in a melodious harmony. And the people lived in a blissful and industrious happiness. And God loved each one of them. And they each gave thanks to God for their life and their joy and their responsibility and even for their sorrow, for sorrow is the test of a man. And particularly they gave thanks for the Great Prophet who had given the country its motto which read "Liberty to Each, Peace and Prosperity to All". And wherever you went in this beautiful country you would find magnificent monuments in stone and steel, in flowers and precious gems proudly proclaiming their joyous heritage.

Now this happy people had only one common sorrow—a certain minor illness had become prevalent among them. And there were great ponderings and meetings and strikings off of committees and statistical reports to decide what should be done. And at last a drug was found which appeared to combat the disease. And the people were jubilant. And they gave thanks to God for the discovery.

But a great controversy arose. And some among them there were who maintained that the drug should be given to all. But the people appealed to their Supreme Court. And the Supreme Court of that happy land pointed to the motto of the Great Prophet (for it formed the basis of their Constitution). And the Supreme Court decided that such was contrary to "Liberty to Each". And the people cheered the decision and their wise Supreme Court. And they were happy.

But there were murmurings amongst those who, carried away by their own vision of freedom from this mild disease, thought they knew better. And they consulted amongst themselves as to how they might have their way. And a plan was formed. And so it came about that one dark and dreadful night they secretly changed the motto. And the motto now read "Liberty, Peace and Prosperity to All". And the change was subtle and slight. And the people heeded it not. But the change spelt death to the individual.

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And gradually a change came over the people also. And the seed of the collective was sown. And the weeds that sprang therefrom choked out the flowers of individuality. And those once happy people were emptied of themselves. And they wandered unknowingly into a lonely and everlasting night—into a faceless anonymity in the amorphous all. And an unhuman humanity was born.

And the cause of "Liberty to Each" was lost forever.
And the Great Prophet wept.
And God despised all that people.

C. P. HARRISON, M.B.

Suite 420,
604 Columbia St.,
New Westminster, B.C.,
March 27, 1958.

THE LONDON LETTER

(From our own correspondent)

NEW CHAIR OF ANÆSTHESIA

By a munificent gift of £150,000 the British Oxygen Company has endowed a chair of anæsthesia at the Royal College of Surgeons, and Dr. Ronald Woolmer, the director of the department of anæsthesia of the College, has been appointed the first occupant of the Chair. This establishment of the first chair of anæsthesia in London is a fitting recognition of the leading position which this country now occupies in the field of anæsthesia. The credit for this is shared equally by the Faculty of Anæsthetists of the College and the Association of Anæsthetists of Great Britain and Ireland who, between them, have been responsible for raising the status of anæsthesia from that of a very humble handmaiden of surgery to that of a specialty of equal status with surgery and medicine. To those of us of the "rag and bottle" generations modern anæsthesia may appear a mysterious maze of awe-inspiring apparatus, but to the patient of today it means the difference between purgatory and paradise.

A NOTABLE OCTOGENARIAN

One of the great names of British surgery—that of Sir Gordon Gordon-Taylor—has now to be added to the ranks of famous octogenarians on March 18. To commemorate the occasion the current issue of the *British Journal of Surgery* is a "Special Gordon-Taylor Birthday Number". In addition, at a pleasing ceremony at his old hospital—the Middlesex Hospital—he has been presented with his portrait. His reputation is, of course, international. He is an honorary LL.D. of Toronto and Melbourne, as well as being an honorary M.D. of Athens and an honorary Fellow of the Canadian, Australian and American Colleges of Surgeons. His dapper figure, always with a carnation in his buttonhole, belies his age, and the twinkle in his eyes is as vivid as ever. A doyen of his art, he carries with him into the new decade upon which he is entering the congratulations and warm good wishes of surgeons and physicians in all parts of the world.

PETS AND VIRUSES

This has been a bad month for pets and their owners. First of all, the virologists of Glasgow published a most impressively circumstantial description of how a fatal case of poliomyelitis in a child had apparently been caused by contact with a sick budgerigar in the household. To show that Scotland was not the only country where such unpleasant ideas could be produced, Dublin came forward with a slightly less convincing, but nevertheless suggestive, story of a canary having been the transmitter of poliomyelitis to man. Soon afterwards, and quite coincidentally, the current issue of the *Proceedings of the Royal Society of Medicine* included an interesting dissertation suggesting that the cat might be the transmitter of the causative organism of infective polyneuritis, or the Landry-Guillain-Barré syndrome. The author reports six personal cases, and three others, in which the onset of the disease was directly related to an illness of the patient's cat. The probable related disease is feline enteritis, from which some 70% of cats suffer at some time or another. In collaboration with Messrs. Burroughs Wellcome, complement-fixation reactions have been carried out on patients who have suffered from infective polyneuritis, using as antigen cat's tissues infected with feline enteritis virus. So far as they have gone, the results "suggest that there is a distinct difference between the patients' blood and that of the controls".

CONTAMINATED EGG PRODUCTS

Equally disturbing has been a report from the Public Health Laboratory Service to the effect that "there can be no doubt that egg products are a fruitful source of salmonella infection in man, and that Chinese products have been a potential and actual cause of outbreaks of paratyphoid fever". The report is based upon the examination of nearly 20,000 samples of egg products. Imported egg products—frozen eggs and yolks, dried egg, and dried and frozen albumen—constitute just under 4% of the total eggs and egg products used in the United Kingdom. In all, 54 strains of *Salm. paratyphi B* were isolated: 19 from frozen whole egg and 35 from dried albumen. Of the frozen whole egg, 0.21%, and of the dried albumen, 0.58% contained this organism, and all of these were derived from Chinese egg products. Analysis of the epidemiological records shows that of 20 phage types of *Salm. paratyphi B* met with in cases of paratyphoid fever during January 1955 to November 1956, eight (the ones found in Chinese egg) had been responsible for 80% of the incidents. From the point of view of prophylaxis, attention is drawn to the fact that none of the 143 samples of Polish egg examined yielded salmonellas, and that the Polish products are all pasteurized.

OCCUPATIONAL MORTALITY

That statistics can sometimes be fascinating is amply demonstrated by the recently published Registrar General's Supplement on Occupational Mortality, which is based on the 1951 census. Shop owners, for instance, have a relatively greater mortality than their assistants from coronary disease and suicide, but the assistants die more often from tuberculosis. Printers and bookbinders have an apparently high death

rate from leukæmia, whilst coal-miners have an exceptionally high standardized mortality ratio (S.M.R.) from cancer of the stomach but exceptionally low ratios for cancer of the lung and poliomyelitis. From the fact that the S.M.R. for doctors is now 89, compared with 106 in 1930-36, it might be argued that the National Health Service has been to the benefit of the profession. Diseases in which doctors have high S.M.R.'s include psychoses, suicide, cirrhosis of the liver, and gallstones and cholecystitis. Although they have a relatively high ratio for coronary disease (159), this is not so very much higher than that for ministers of religion (152) and lawyers (121).

WILLIAM A. R. THOMSON

London, April 1958.

ABSTRACTS *from current literature*

MEDICINE

Cytologic Patterns in Bronchopulmonary Disease.

A. A. CARABELLI: *Am. Rev. Tuberc.*, 77: 22, 1958.

A study of the bronchial aspirate or irrigate in a series of 1000 cases of bronchopulmonary disease was made by the Papanicolaou technique to determine the presence of pathognomonic cytograms.

This study revealed three large categories of bronchopulmonary diseases which may be said to have a characteristic cytogram: acute and chronic suppurative bronchopneumonitis with the leukocyte prominent or predominating; acute and chronic allergic bronchopulmonary disease with eosinophils present or prominent; neoplastic bronchopulmonary disease with malignant cells.

The cytogram of acute or chronic suppurative bronchopneumonitis may be superimposed on either the allergic or the neoplastic groups to mask the underlying disease. A peculiar pseudomalignant group of cells easily mistaken for malignant epidermoid types, which is present in the bronchopulmonary suppurative group and occasionally in the allergic group, is described.

In spite of the fact that this study appears to give a discrete description of three large groups of diseases with what appear to be pathognomonic cytograms for each group, frequent overlapping was noted when some form of suppuration was superimposed on either the allergic or the neoplastic groups. It may be possible to miss the basic diagnosis entirely if only one section of a smear is studied. Suppuration is a common complication in these diseases. On the other hand, the finding of a suppurative cytogram does not preclude the presence of other diseases such as tuberculosis or fungal infections.

Special attention was paid to pulmonary tuberculosis. In the early uncomplicated cases there was nothing characteristic in the cytogram, and only normal cells were noted. Most tuberculous foci studied presented a complicating suppurative process of some type, but none of the cytograms indicated anything characteristic of tubercle bacilli in the aspirate or irrigate.

S. J. SHANE

Diverticulum of the Pericardium with Observations on the Mode of Development.

H. C. MAIER: *Circulation*, 16: 1040, 1957.

The evidence concerning the mechanism of development of a diverticulum of the pericardium is discussed on the basis of two personally observed cases, some experimental autopsy observations, and an analysis of cases recorded in the literature. The development of a large diverticulum that was not roentgenographically demonstrable until some years after an attack of idiopathic pericarditis is recorded. Although congenital factors may play a predisposing role by providing a weak area in the parietal pericardium, an increase in intrapericardial pressure with pericardial effusion seems to be the important causative factor in many cases. A pericardial diverticulum usually results from the gradual stretching of a herniating portion of the inner serous layer of the parietal pericardium that bulges through the split or weakened outer fibrous layer of pericardium.

Evidence supporting the concept that pleuropericardial cysts and a pericardial diverticulum may have a common origin is indicated by a case in which both lesions were associated. However, congenital diverticulum of the pericardium seems to be extremely rare.

It is questionable whether a pericardial diverticulum would usually require any therapy if a positive diagnosis could be established by radiologic and clinical criteria. At present it seems unjustified to assume that the radiologic features that have been described and discussed in the literature are sufficiently accurate to be considered diagnostic or reliable except in rare instances. Although alterations in the shape and contour of a pericardial diverticulum may be noted with changes in position or respiratory motion, similar variations may occur in pleuropericardial cysts and even in other lesions. Therefore the management of the patient must be based on a realization of the limitations of radiographic differentiation of the large variety of mediastinal masses and vascular lesions that could simulate a pericardial diverticulum. Angiography will help to identify lesions of the heart and great vessels. When the radiographically detected mass is considered to be of nonvascular origin, thoracic exploration is advisable unless other conditions produce contraindications.

S. J. SHANE

Heart Disease of Pulmonary Origin.

G. R. HERRMANN AND A. H. SHIELDS: *Dis. Chest*, 33: 52, 1958.

Criteria for definite diagnosis of pure, chronic cor pulmonale are set down and the findings in 51 patients who meet these qualifications are described. By far the greatest incidence is in middle-aged white males, though it is seen in all ages, both sexes, and various racial groups. The electrocardiogram shows the changes rather late, and in general is of relatively little value in assessing the degree of cardiac change; yet the electrocardiographic finding may be the first to focus attention on the presence of a right ventricular overload. Detailed blood volume studies are described in 17 patients with cor pulmonale and six persons with emphysema, using radioactive iodinated human serum albumin to determine plasma volume, and Cr^{51} for estimation of the total red blood cell mass. The emphysema patients were consistently abnormal, but those with definite cor pulmonale

showed a variable increase of total blood volume and a consistent increase of red blood cell mass. Follow-up studies after digitalization of patients with failure showed decrease in plasma volume invariably, and frequently a marked inexplicable decrease of red blood cell mass.

In management of these patients, the authors strongly emphasize the importance of prophylaxis, early recognition, and energetic treatment in the early phases, even before cardiac changes are manifest. It must be admitted that the patients who meet the usual criteria represent the most advanced and refractory ones. While the long-term prognosis is poor, current drugs and practices offer the patient comfort, ability to work, and probably a longer life span than was previously possible. S. J. SHANE

Testicular Feminization in Adults *(in German).*

G. A. HAUSER *et al.: Schweiz. med. Wchnschr.*, 87: 1573, 1957.

This little known intersexual state is well defined and can be diagnosed clinically with a great degree of accuracy. Its main symptoms and signs are: primary amenorrhœa and sterility, resistant to treatment; short vagina with blind end, occasionally absent altogether; scanty or missing pubic and axillary hair—"hairless woman"; absence of uterus; inguinal hernias; presence of testes usually in the hernias; preponderantly masculine type of chromosomes.

The authors report six cases of this condition and describe in detail the physical findings and endocrine status with hormone determination, including chromatograms of 17-ketosteroids. Neutral 17-ketosteroid excretion was that of normal men. Œstrogen output was diminished and FSH levels were normal. Microscopic examination of the testes removed at operation is described and the findings are discussed.

The authors are opposed to routine removal of the testicles because this is followed by severe withdrawal symptoms. They do not ignore the possibility of malignant change in these testes, but believe that it is much less frequent than in ordinary cases of cryptorchism.

Testicular feminization is regarded as a testicular insufficiency, which in its less extreme form may express itself merely as a hypospadias. Various degrees of pseudo-hermaphroditism may be encountered. The length of the vagina can serve as a measure of the degree of testicular insufficiency. W. GROBIN

Effects of Smoking Upon the Mechanics of Breathing. I. In Normal Subjects.

E. O. ATTINGER, M. M. GOLDSTEIN AND M. S. SEGAL: *Am. Rev. Tuberc.*, 77: 1, 1958.

In experiments in humans and dogs, the œsophageal balloon method was found to be a valid replacement for direct intrapleural pressure measurements under the influence of drugs and stress conditions, and it was employed for the determination of pressure-flow and pressure-volume relationship in these studies.

The mechanics of breathing in 20 normal subjects (9 nonsmokers and 11 smokers) were studied before and after smoking one or two cigarettes. There were *no statistically significant differences* in the mechanics of breathing between smokers and nonsmokers in the control state. Although some subjects showed changes in the mechanics of breathing, statistically indicative of the appearance of unequal ventilation, there was no difference between the control state and the post-smoking state. S. J. SHANE

Effects of Smoking Upon the Mechanics of Breathing. II. In Patients with Cardiopulmonary Disease.

E. O. ATTINGER, M. M. GOLDSTEIN AND M. S. SEGAL: *Am. Rev. Tuberc.*, 77: 10, 1958.

Smoking one or two cigarettes did not produce any significant changes in mechanical resistance, pulmonary compliance, or the work of breathing in normal subjects and in patients with rheumatic heart disease.

The total number of persons in each of the three main groups studied permits valid statistical analysis. The over-all results in the normal subjects and in patients with cardiac disease fail to show *any marked difference* between smokers and nonsmokers. An increase in mechanical resistance was noted in the smokers in the pulmonary disease group. The harmful physiologic effects of smoking noted in some patients therefore seem to depend upon the individual. These effects may be accentuated in patients with *chronic* involvement of the tracheobronchial tree, such as those seen in chronic pulmonary emphysema.

These findings are somewhat surprising in the light of the clinical findings in the literature. In essence, they confirm the results of certain previous workers who found a marked increase in mechanical resistance in patients with chronic pulmonary emphysema, but no changes in normal subjects.

Any difference noted between smokers and nonsmokers in the control state would indicate the *chronic* effects of smoking upon the mechanics of breathing, provided the groups are otherwise comparable.

S. J. SHANE

The Diagnostic Approach to Hypertension due to Unilateral Kidney Disease.

A. A. BRUST AND E. V. FERRIS: *Ann. Int. Med.*, 47: 1049, 1957.

Attempts to establish a diagnostic relation between hypertension and suspected or demonstrated renal lesions are reviewed in the light of the authors' experience with 14 hypertensive patients. Eleven presented themselves with accelerated and three with benign hypertension as judged by the clinical picture. On the basis of the pathological condition of the kidneys, the patients were classified as suffering primarily from vascular lesions (nine cases) or from parenchymal lesions (five cases).

Nephrectomy was carried out in five of the patients with vascular lesions, and resulted in "cure" of the hypertension in four. All of the five patients with parenchymal lesions were also subjected to nephrectomy, but the hypertension continued after the operation. Four of the patients of this last group had unilaterally diseased kidneys that were contracted, nonfunctioning and pyelonephritic.

Accepted methods of study, such as urinalysis, intravenous and retrograde pyelography and the usual tests of differential renal function, proved disappointing. Despite the risks associated with aortography, this method was used and provided a delineation of vascular lesions which otherwise would have escaped observation.

Lack of blood-pressure response to a ganglionic-blocking agent (tetraethylammonium chloride) was noted before operation in the cases of patients who

were ultimately "cured" by nephrectomy, while the patients who underwent "unsuccessful" surgery showed responses to tetraethylammonium chloride similar to those of the general hypertensive population. These results suggest that tests with ganglionic blocking agents can provide information useful from three points of view:

1. They may possibly aid in the identification of patients in the general hypertensive population who are suspected of having a humoral basis for their hypertension.

2. They may also aid in the characterization of hypertension as a phenomenon originating in the kidneys in cases in which unilateral renal lesions have been demonstrated.

3. The data in this study also suggest that a regularly occurring pressor response or lack of blood-pressure fall after the administration of a ganglionic blocking agent in cases of unilateral renal hypertension, may indicate that the hypertensive process is reversible.

S. J. SHANE

Ebstein's Anomaly: Presentation of Ten Cases.

F. E. MAYER, A. S. NADAS AND P. A. ONGLEY: *Circulation*, 16: 1057, 1957.

The findings in 10 cases of Ebstein's anomaly of the tricuspid valve are correlated with those reported in the literature to emphasize certain clinical features of diagnostic value. Symptomatology is usually mild with cyanosis, dyspnœa, fatigability, and commonly a history of bouts of palpitation. The physical findings are characterized by normal growth, frequent cyanosis and infrequent clubbing; a quiet cardiac impulse and a systolic thrill between xiphoid and apex; a triple or quadruple rhythm, a second sound diminished at the pulmonary area, and a combination of systolic and diastolic murmurs maximal at the lower left sternal border or apex. Phonocardiographic studies confirm the presence of a triple or quadruple rhythm, show a delayed first sound of normal intensity, demonstrate a systolic murmur of moderate intensity and medium frequency, and a presystolic murmur at the lower left sternal border and apex. Mid-diastolic murmur in this area is less constant. The characteristic electrocardiogram has tall P waves, frequently prolonged atrioventricular conduction, considerable right bundle-branch block, and right ventricular potentials of low amplitude. By radiologic examination marked cardiomegaly is seen, a contour consistent with right-sided enlargement, a narrow base, diminished pulmonary vascular markings, and poorly delineated pulmonary artery. Angiocardiography reveals a huge right atrial chamber with delayed emptying, poorly opacified pulmonary radicles, and frequent evidence of a right-to-left shunt. Cardiac catheterization demonstrates a large atrium, displacement of the tricuspid valve to the left, moderately elevated right atrial pressure, normal right ventricular systolic pressure and absence of a significant gradient across the pulmonary valve. Peripheral arterial oxygen unsaturation is usual.

The importance of clinical recognition of this entity is stressed in view of the definite hazard involved in undertaking cardiac catheterization and surgical procedures in these patients. Several patients have died during or shortly after cardiac catheterization. If the condition is suspected, this mode of investigation should be avoided.

S. J. SHANE

SURGERY

Regurgitation Cholecystitis and Cholelithiasis.

A. M. LARGE: *Ann. Surg.*, 146: 607, 1957.

During animal experiments on reconstruction of bile ducts, it was found that when the sphincter of Oddi was cut or bypassed, infection was likely to localize in the gall-bladder and this was often accompanied by gall-stone formation. This infection appeared to be due to regurgitation, for it did not involve the duct walls or periductal lymphatics. Nor were infection and stone formation severe if the gall-bladder was removed. Clinical case reports are submitted to confirm that the same phenomenon occurs in humans. It also occurs when the intestine is anastomosed to the fundus of the gall-bladder.

Wherever a wide opening is made between the common bile duct and the intestine, the gall-bladder should be removed, even if it is perfectly normal.

BURNS PLEWES

Improved Management of Clinical Hypothermia Based upon Related Biochemical Studies.

W. G. WADDELL, H. B. FAIRLEY AND W. G. BIGELOW: *Ann. Surg.*, 146: 542, 1957.

Since 1952, 323 patients have been operated upon in University of Toronto hospitals at body temperatures below 31°C. Biochemical studies of 46 adult cardiovascular cases have been made in the investigation of re-warming "shock", ventricular irritability and increased bleeding tendency.

The technique of cooling is by cooling blankets and ice over periods up to 1½ hours under general anæsthesia. Œsophageal and rectal temperatures, electrocardiographic tracing, and blood pH are monitored. Re-warming may take several hours and occasionally the radio-frequency device developed with the help of the National Research Council of Canada is used.

Problems encountered during re-warming of patients after surgery with hypothermia have been related to the development of metabolic acidosis and are controlled by modifying the anæsthetic technique. An attempt has been made to maintain patency of the vascular tree and control shivering by the use of chlorpromazine, promethazine and meperidine. There is evidence that heparinized blood is superior to citrated blood for transfusion during hypothermia. It has reduced the incidence of irreversible ventricular fibrillation.

A reversible acute thrombocytopenia has been observed at low body temperatures. This study has not contributed to the management of the occasional severe bleeding tendency encountered in hypothermia.

In 75 pædiatric and adult cases of open heart surgery with hypothermia, there were four deaths, a mortality rate of 5.3%.

BURNS PLEWES

Follow-up on 200 Patients Treated for Hirschsprung's Disease During a Ten-year Period.

O. SWENSON: *Ann. Surg.*, 146: 706, 1957.

The lesion in Hirschsprung's disease is postulated to be a dysfunction of the terminal colon segment. No ganglion cells are present in this region but the proximal dilated colon is normal. This resulted in treatment by resection of the rectum and rectosigmoid and a low anastomosis—a difficult operation.

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In 200 consecutive patients who had resection of the aganglionic segment there were six postoperative deaths. A mortality of 3% among such malnourished and ill children seems acceptable, but the rate is lower since the use of colostomy to delay resection till 12 to 18 months of age. Operation should be done during a stage in which the child can co-operate in colonic elimination.

Out of a group of 73 patients followed up for 5 to 10 years, all but one are completely relieved of symptoms. Incontinence is not a problem. The rest of the 196 patients are also in a satisfactory state. Only five of the whole group have had chronic recurrent diarrhœa. Seven children have died from one to five years after operation with an illness of less than 24 hours duration and with severe dehydration. There is no evidence that the operation results in a defect in ejaculation. A number of the patients have become fathers. The resection should be carried down to within 2 cm. of the anal canal to obtain good results.

BURNS PLEWES

Care of the Severely Injured Patient—Urologic Aspects.
J. H. DE HEERD: *J. A. M. A.*, 165: 1916, 1957.

The author stresses the usefulness of excretory urography as soon as the patient's general condition will permit, pointing out that in addition to helping in assessing damage to the injured kidney it also shows the status of the contralateral organ. This is of paramount importance if nephrectomy is to be considered. He points out that function, although reduced, is rarely absent, unless the entire kidney has been avulsed from its arterial supply. He is against immediate cystoscopic and retrograde examination in most cases.

A conservative regimen is usually advocated except where the roentgenographic and clinical picture indicates irreparable damage. It is pointed out that untimely surgery may break down the natural controlling barriers to hæmatoma, and once started may leave nephrectomy as the only alternative. Several interesting radiographs are presented showing that, even in cases of severe renal damage, good function with relatively normal caliceal and renal architecture ultimately ensued.

The importance of careful analysis, including use of digital rectal examination, is emphasized in respect to bladder and posterior urethral injuries. Conventionally accepted methods are discussed. The desirability of early realignment of the divided urethra and replacement of the prostate is mentioned, along with an illustrated description of the standard use of the Davis interlocking sounds. It is suggested that a silk suture placed in the eye of the traction catheter and brought out through the suprapubic wound will aid in replacing the catheter should the balloon burst. The catheter in this type of case should remain in position for approximately four weeks.

A. M. DAVIDSON

Care of the Severely Injured Patient—Neurosurgical Injuries.
J. C. WHITE: *J. A. M. A.*, 165: 1924, 1957.

The author deals with the clinical and pathological picture of neurosurgical injuries, and their treatment. He reminds us of the usefulness of a small plug of cotton in the foramen spinosum in those cases of middle meningeal arterial hæmorrhage which cannot otherwise be controlled. In cases where the brain fails to expand after the clot has been removed, he is in favour of Gillingham's method of forceful injection of 100 c.c. of isotonic sodium chloride solution from below by lumbar puncture. He feels, however, that in most cases sectioning of the tentorium to disimpact an uncal herniation is likely to cause more harm than good. The practice of bilateral temporal trephining is advocated where rapidly deepening coma seems indicative of brain stem compression, even in the absence of cranial fractures. Often most of the cerebral damage is of a contrecoup nature. Similarly, suboccipital decompression is recommended if it seems that respiratory failure is attributable to fractures which enter the foramen magnum or the crossing of the major venous sinuses.

Tracheotomy is a very useful adjunct in many head injuries and adds 100 c.c. or more to respiratory exchange. In spinal cord injuries, hæmorrhage and œdema may extend cephalad and paralyze the anterior horn cells of the phrenic nerve. With diaphragmatic breathing alone, the vital capacity may be reduced to about 500 c.c. During the first few days after cervical injuries, operation is especially hazardous because of the vasomotor instability and lowered respiratory function.

A. M. DAVIDSON

Identification of Cause of Obscure Massive Upper Gastro-intestinal Hæmorrhage During Operation.
M. P. OSBORNE AND J. E. DUNPHY: *A.M.A. Arch. Surg.*, 75: 964, 1957.

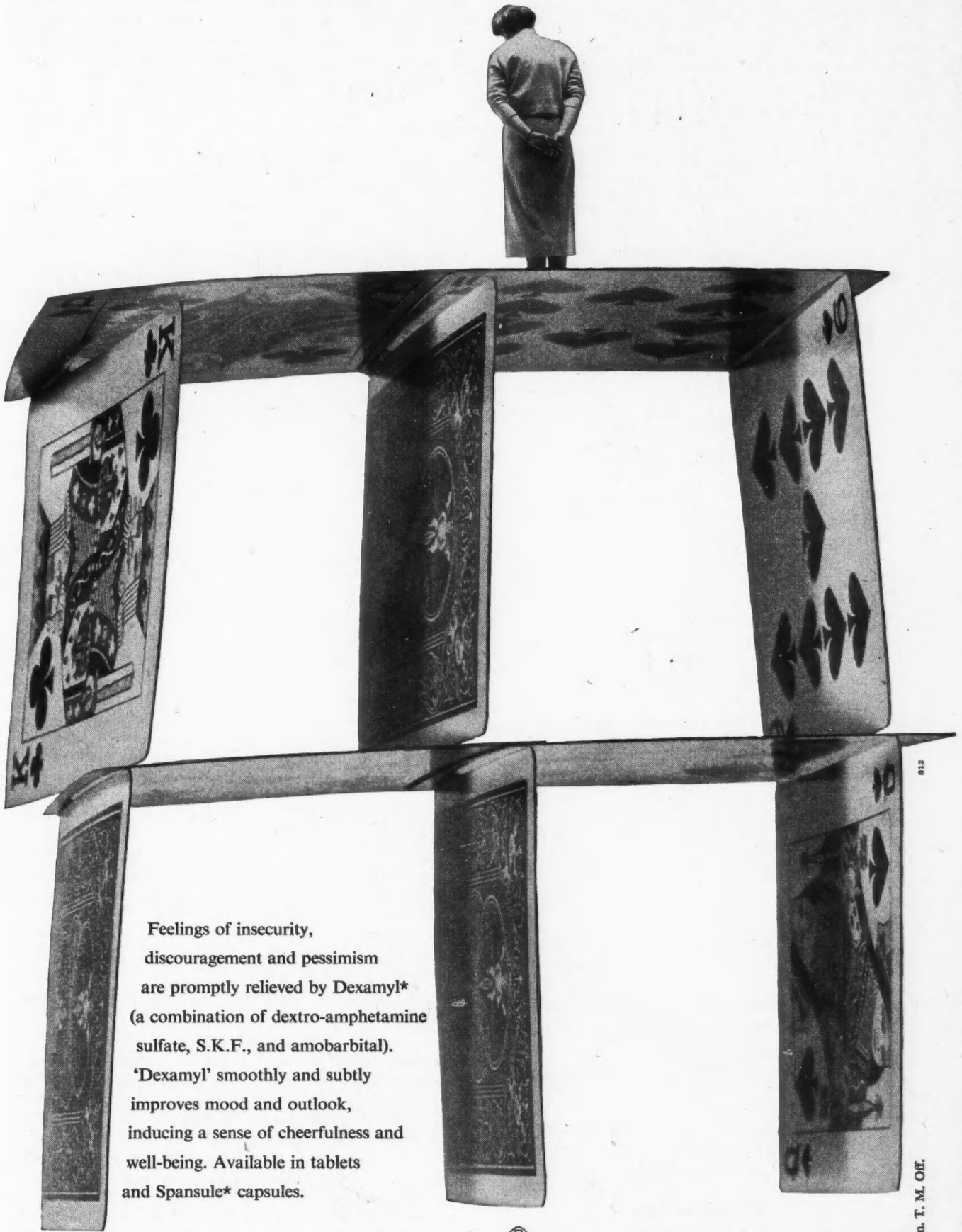
Severe bleeding from the upper gastro-intestinal tract presents a severe problem in many cases in spite of the use of limited x-ray studies, evaluation of liver function, œsophagoscopy and even gastroscopy. Often laparotomy must be undertaken without a confident preoperative diagnosis. An operative technique is presented for use in such cases. The clotting of the blood in the incision, presence of portal collateral circulation, ascites, liver consistency, etc., are noted on opening the abdomen. The stomach, œsophageal hiatus, duodenum and spleen are inspected. The lesser sac is opened and the posterior gastric wall is palpated. The duodenum is mobilized for better examination. The upper small bowel is examined by palpation and transillumination. If the source of bleeding is still undiscovered, a gastrotomy is done, inverting the fundus and duodenum into the opened stomach for better examination. A lesion of the 2nd or 3rd portion of the duodenum may be suspected if blood flows back from beyond the visualized area. The small bowel and colon are examined if all this fails. (Bleeding submucosal jejunal aneurysm is described.)

In 100 consecutive cases operated upon at the Boston City Hospital, only two had an unknown source of bleeding finally. Gastrotomy was necessary to establish the diagnosis in 26. In seven cases a "blind gastrectomy" was done, with success in controlling the hæmorrhage in four (a mortality of 42%). Cases are described in which the bleeding gastric ulcer was just proximal to the transection of the stomach.

Gastrotomy rather than "blind gastrectomy" is recommended.

BURNS PLEWES

(Continued on page 732)



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(Continued from page 730)

OBSTETRICS AND GYNÆCOLOGY

Rupture of the Marginal Sinus of the Placenta.
J. H. FERGUSON: *J. A. M. A.*, 166: 476, 1958.

Rupture of the marginal sinus is one of the most frequent causes of bleeding in the later weeks of pregnancy. There is a growing appreciation of its existence. It is not particularly dangerous for the mother or baby. Rather, its importance lies in the necessity of differentiating it from abruption, low-lying placenta, and minor degrees of placenta previa, so that these diagnoses can be more accurately catalogued. In particular, a clearer picture of abruption should emerge from a wider understanding of rupture of the marginal sinus. The diagnosis of rupture of the marginal sinus of a normally located placenta depends on a demonstration at the margin of the placenta of a clot continuous with clotted blood in the marginal sinus. At the same time it must be demonstrated that the clot had not interposed itself between the uterus and the placenta.

ROSS MITCHELL

Use of Newer Progestins in the Treatment of Endometriosis.
R. W. KISTNER: *Am. J. Obst. & Gynec.*, 75: 264, 1958.

Based on the assumption that normal pregnancy improves endometriosis both subjectively and objectively, a state of "pseudopregnancy" has been induced for treatment of this condition by administration of large doses of œstrogen and progestins for periods of two to seven months. It is suggested that the changes brought about in endometriosis by pregnancy are a combination of: (1) anovulation and amenorrhœa; (2) decidual transformation of functioning endometriotic tissue; and (3) decidual necrosis and absorption.

Decidua was produced in the endometrium of all patients as determined by endometrial biopsies, and in the areas of endometriosis of the one patient subjected to operation at the end of treatment. Nine patients were subjectively and objectively improved during the period of pseudopregnancy.

No conclusions can be drawn regarding the long-term effect of this treatment at the present time. Variations in dosage of both œstrogens and progestins will be necessary for optimum effect. The use of this method as prophylaxis against the development of endometriosis is discussed.

ROSS MITCHELL

Radiation Hazards in Obstetrics and Gynæcology.
S. S. PARLEE: *Am. J. Obst. & Gynec.*, 75: 327, 1958.

Because of the publicity, particularly in the lay press, there has been much confusion in the public mind, and indeed in the minds of physicians, regarding the effects on the human race of exposure to various ionizing rays, particularly gamma rays. On the one hand these rays are valuable diagnostic and therapeutic weapons. On the other hand they have some carcinogenic and detrimental genetic effects. These two aspects of the rays must be seen in their proper perspective. It appears that no woman in her reproductive years, and more particularly no woman who is pregnant, should be x-rayed without a proper indication. It seems equally clear that neither should these rays be withheld in such a woman if a valid indication exists. If she is x-rayed, it should be done at a time when the most information can be obtained from this procedure. When she is x-rayed, all adequate precautions should be taken to avoid excessive and unnecessary radiation. Few of us are much interested in our descendants 40 generations hence, but we do have some responsibility to posterity.

ROSS MITCHELL

THERAPEUTICS

Spectrophotometric Determination of Para-Aminosalicylic Acid in Blood and Urine.
P. A. CACCIA: *Am. Rev. Tuberc.*, 76: 1071, 1957.

The large doses of sodium PAS administered to patients, the rapid elimination of the drug from the blood, and the large amount found in the urine, together with isoniazid or pyrazinamide, require the development of a method which is specific and, at the same time, sensitive to about 1 μg. per ml.

A colorimetric method for the determination of para-aminosalicylic acid (PAS) sodium salt in blood and in urine is described. Normal constituents of blood and urine do not interfere with colour reaction which is specific for PAS because of NH_2 and OH in the meta position. The sensitivity of the test is 0.5 to 1 μg. per ml. The colour develops slowly, reaches its maximal intensity after one hour, and then remains stable for several hours.

S. J. SHANE

Pyrazinamide and Cycloserine in Treatment of Pulmonary Tuberculosis.
W. S. SCHWARTZ AND R. D. MOYER: *Am. Rev. Tuberc.*, 76: 1097, 1957.

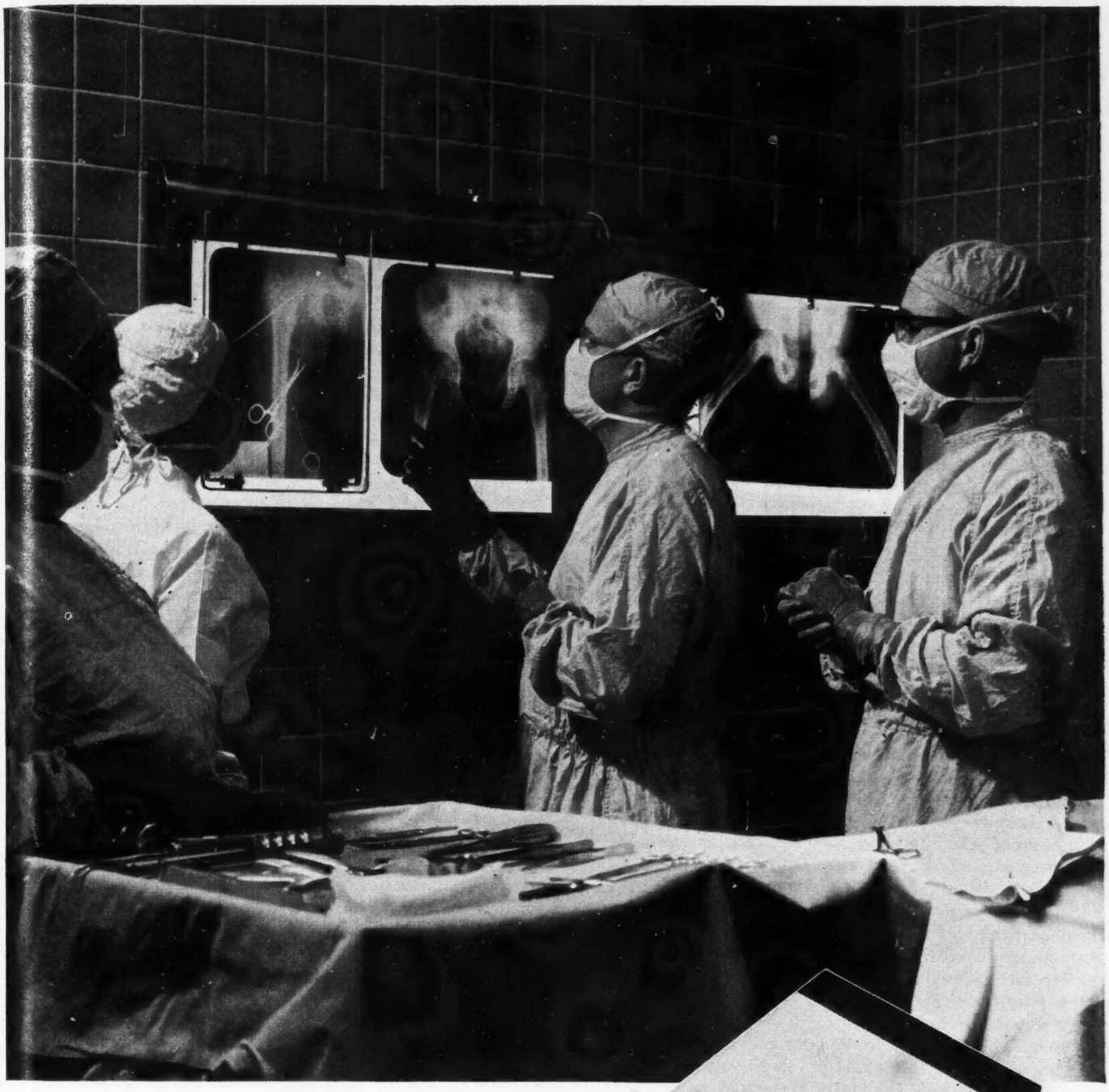
Forty-four patients with moderately or far advanced active pulmonary tuberculosis which had not been successfully treated received therapy consisting of 3 g. of pyrazinamide and 0.5 g. of cycloserine each day for periods ranging from 12 days to more than 10 months. Hepatotoxicity associated with pyrazinamide occurred in 15% of the group. There was no clear-cut instance of toxicity attributable to cycloserine. It appeared that the combination of pyrazinamide and cycloserine was not superior to either cycloserine or pyrazinamide given as single drugs, when judged by roentgenographic change, reversal of infectiousness, and delay in the emergence of cycloserine-resistant organisms.

S. J. SHANE

Influence of Anticoagulants on Cerebral Infarction Produced by Homologous Blood Clots.
S. H. FRAZIER *et al.*: *Proc. Staff Meet. Mayo Clin.*, 32: 717, 1957.

Cerebral infarcts developed in 20 of 29 dogs (69%) in which injection of 48-hour-old homologous clots was made into the internal carotid artery in the neck and in which the prothrombin activity had been reduced by administration of dicoumarol. The proportion of animals in which infarcts developed is almost equal to that for a control group that did not receive anticoagulants. This indicates that reduction in prothrombin activity did not reduce the occurrence of experimental infarction by this method. The effect of the anticoagulants on the hæmorrhagic component of the infarcts in the experimental group was approximately the same as that on those infarcts in the

(Continued on page 734)



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(Continued from page 732)

control group which ordinarily had a hæmorrhagic character. S. J. SHANE

Staphylococci: Ubiquitous Nature of Human Infections and their Control by Antimicrobial Agents.
P. BUNN *et al.*: *Ann. Int. Med.*, 48: 102, 1958.

This report is concerned with a description of laboratory methods designed to demonstrate the efficacy of a substitute for penicillin, and clinical experiences with the best of the substitutions so far observed. Although hardly comparable with respect to numbers of organisms killed and the speed of killing, *erythromycin and chloramphenicol* in combined large dosage has proved to be an effective combination to control growth of penicillin-resistant organisms. These two, with perhaps bacitracin for a few days, have proved to be as effective a combination in therapy of human infections as has been described. No other single drug or combination of them (antimicrobial therapy) has been shown to be better, consistently at any rate.

It has been the impression of the authors, both *in vitro* and *in vivo*, that staphylococci whose resistance to penicillin is greater than 0.15 u./ml. *produce penicillinase*, and are, for practical purposes, penicillin-resistant. Penicillin in clinical therapy is useless in infections caused by those strains of staphylococci. Similarly, other single-drug therapy has resulted in increasing numbers of strains of staphylococci resistant to multiple other agents. In such circumstances the agent is of no clinical value either.

Irrespective of the importance of the epidemiologic aspects of penicillin-resistant staphylococci, it cannot be concluded that the infection hits only old persons in the hospital whose admission was necessitated by some other debilitating, noninfectious disease. Although uncommonly seen in a setting of good health, penicillin-resistant staphylococcal infections occur at all ages, in patients well removed from exposure to hospital personnel and without known exposure to a contaminated source. They do, however, probably occur more often in patients receiving antibiotics for some non-specific "prophylactic" reasons than in patients not so "protected."

Energetic but not unreasonably radical therapy for disseminated penicillin-resistant staphylococcal infections is indicated. A significant reduction in mortality is anticipated, although the lowering is not so great as had been hoped for. To date, no agent or combination of them is as efficacious as penicillin was in the era when the majority of isolated strains were sensitive to it. Adjuvant therapy is essential if there is localization of the infection; with pus, surgical drainage is required.

Although the erythromycin-chloramphenicol combination is partially effective, a better combination can be anticipated. It is hardly likely, though, that such a combination will be prefabricated into a single capsule or vial. Manipulation of dose of each most assuredly will always be needed.

Staphylococcal sepsis caused by strains resistant to penicillin and other antibiotics is *not a hopeless infection;* specify therapy with antimicrobials, along with proper adjuvant therapies, can be expected to lower the present mortality rate. Inevitably a more powerful agent or agents, or a better grouping of one now available, will be found which will interrupt rapidly and more completely the pathogenic career of penicillin-resistant staphylococci in human infections.
S. J. SHANE

Pyrazinamide and Viomycin in the Surgical Treatment of Pulmonary Tuberculosis.
D. V. PECORA: *Am. Rev. Tuberc.*, 77: 83, 1958.

The evidence obtained from the series of patients in this study indicates that the results of surgical resection performed under the protection of pyrazinamide in combination with viomycin or PAS, and probably other antituberculous drugs, are superior to the results obtained with pyrazinamide alone. The results of such multiple-drug therapy also appear superior to the reported results of viomycin alone. The comparatively low incidence of late unsatisfactory results in the group of patients with resections who received multiple-drug therapy would seem to support the impression that drug resistance was delayed beyond the period when it might have emerged had each drug been used alone.

Since such multiple-drug therapy seems to offer prolonged protection, an attempt has been made to employ two drugs to cover surgery whenever possible. In addition to the combinations reported here, regimens including cycloserine, thiosemicarbazone and a sulfone are being evaluated.

When planning pulmonary resection it would seem advisable to substitute for existing drug regimens two new drugs or two drugs to which the patient's tubercle bacilli are known to be susceptible when there is evidence that the patient's organisms are resistant to present antimicrobial therapy. S. J. SHANE

Œstrogen Replacement Therapy in Women with Coronary Atherosclerosis.
R. W. ROBINSON, W. D. COHEN AND N. HIGANO: *Ann. Int. Med.*, 48: 95, 1958.

Significant differences of serum lipid patterns have been demonstrated in normal women of various ages. The serum lipid patterns observed in women with coronary heart disease were not significantly different from those of clinically normal post-menopausal women save for an increased β-/α-lipoprotein-cholesterol ratio. Previously hysterectomized women with coronary heart disease were treated with a high dosage schedule of 5 or 10 mg. of Premarin daily for from two to 31 months. There was a dramatic serum lipid response as early as one month, with a reduction of the cholesterol-phospholipid and β-/α-lipoprotein-cholesterol ratios to levels comparable to those of normal young women within three months. A low dosage schedule revealed that 1.25 mg. of Premarin daily adequately reduced the cholesterol-phospholipid and β-/α-lipoprotein-cholesterol ratios in women whose ratios were initially below the group mean. In women with ratios initially above the group mean, this dosage failed to achieve a comparable level. An increase of dosage to 2.5 mg. daily resulted in a satisfactory lowering of the cholesterol-phospholipid ratio, although the β-/α-lipoprotein-cholesterol ratio remained somewhat elevated. Complications of œstrogen therapy were not serious. They included breast tenderness, recurrence of migraine and nocturnal leg muscle cramps. Breast tenderness was temporary, but either migraine or leg cramps, when sufficiently severe, made necessary the cessation or decrease of œstrogen dosage. S. J. SHANE

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OBITUARIES

DR. CHARLES APPELBE, 59, died at his home on March 15. He was born at Parry Sound, Ont., and entered Queen's University, Ont., in 1915. In the First World War he volunteered for overseas service and served with the Royal Navy from 1916 to 1919. He graduated in medicine from Queen's University in 1924 and took a postgraduate course at the University of Michigan. In 1925 he opened his practice at Parry Sound. He was on the staff of the Parry Sound General Hospital and was medical health officer for Parry Sound and McDougal Township. In 1945 he became a Fellow of the Royal College of Surgeons of Canada.

Dr. Appelbe is survived by his widow and two daughters.

DR. JOHN CAMPBELL ARMOUR, Montreal surgeon, died from a heart attack on March 13 at the age of 62. He was born in Perth, Ont., and studied medicine at McGill University where he obtained his M.D. and M.Sc. degrees. He went to the University of Edinburgh, Scotland, to do postgraduate work. On his return to Canada he lectured in anatomy at the University of Manitoba before resuming practice in Montreal. He was staff surgeon at the Royal Victoria Hospital and assistant professor of surgery at McGill University until his retirement from that post in 1957. In 1947 Dr. Armour became a Fellow of the Royal College of Surgeons of Canada. He was a member of the Canadian Medical Association, the Montreal Medico-Chirurgical Society and the Association of Surgeons of the Province of Quebec.

He is survived by his widow, a son and a daughter.

DR. G. L. BELL of Sioux Lookout, Ont., died on March 8. He was born at Oro Station, near Barrie, Ont., and received his medical education at the University of Toronto, graduating in 1920. During both the First and Second World Wars he served as a Surgeon Lt.-Cdr. with the navy. Dr. Bell had practised medicine at Sioux Lookout for 40 years and was medical health officer and district coroner for a number of years.

He is survived by his widow, one son, Dr. K. Bell, and one daughter.

DR. JOHN NELLES GARDINER, ear, nose and throat specialist, died at his home in Toronto on March 21 at the age of 71. He was born in Kingston, Ont., and received his medical education at Queen's University, graduating in 1910. He spent two years in New York doing postgraduate work and returned to Toronto in 1913. During World War I he served with the Royal Canadian Army Medical Corps.

Dr. Gardiner is survived by his widow and two sons.

DR. HUGH McGAVIN, 83, died at his home on March 8. He was born in Paisley, Ont., and in 1877 his family moved to Manitoba. He received his medical education at the Manitoba Medical College, graduating in 1902. He set up practice in Plum Coulee, Man., where he remained until his death. At one time he was health officer for the municipality of Rhineland.

He is survived by his widow, one son and one daughter.

DR. J. FRASER MacIVER, 72, died on March 16. He was born in Gould, Que., and received his medical education at Queen's University, Ont., graduating in 1913. In 1915 he began to practise medicine in Newport, Vermont, and in 1917 he moved to Montreal. In 1921 he was appointed to the staff of the Montreal General Hospital and at the time of his death was an honorary staff member and governor of the hospital. In 1928 Dr. MacIver went to the Heart Hospital, London, Eng., to do postgraduate work and in 1944 he was certified as specialist in internal medicine by the Royal College of Physicians and Surgeons of Canada. For many years he was honorary physician to the St. Andrew's Society, of which he was a member, and was chief examiner for the London Life Insurance Company in Montreal.

He is survived by his widow and three daughters.

DR. ADAM F. MENZIES, 70, prominent Manitoba physician, died on March 8. He was born at Listowel, Ont., and studied medicine at the University of Manitoba, graduating in 1914. After graduating, he enlisted in the Canadian Army and served overseas. He was awarded the Military Cross while serving in France and he also received a decoration from the Czechoslovakian government. After his discharge from the army in 1919 he set up practice in Morden, Man., where he remained until his death. He won the Chown prize for surgery on graduation and in 1957 he was awarded an honorary LL.D. degree by the University of Manitoba.

Dr. Menzies is survived by his widow, and by two sons and two daughters of his first marriage.

DR. GERARD MICHAUD of Chicoutimi recently died at the age of 54. He was director of the Medical Services of the Aluminum Co. of Canada, Arvida plant. Dr. Michaud was born in Kamouraska and was a graduate of Laval University. He had been assistant medical director of the Lac Edouard Sanatorium from 1930 to 1936 and later Medical Director of the Roberval Sanatorium. He was a Fellow of the American College of Chest Physicians and Consultant at the Hôtel-Dieu St-Vallier, Chicoutimi.

DR. GEORGE H. MURPHY, well-known surgeon, teacher and writer, died suddenly at his home on March 7 at the age of 82. He was born in Antigonish County, N.S., and studied medicine at the Halifax Medical College, graduating in 1902. He started in general practice in Dominion, N.S., and served as surgeon to St. Joseph's Hospital, Glace Bay. In 1906 and 1907, Dr. Murphy undertook postgraduate work in London, England, and in 1914 he moved to Halifax. During his surgical career he was surgeon at the Halifax Infirmary, and chief of one of the surgical services of the Victoria General Hospital. In 1930 he became Nova Scotia's first Minister of Health, and during his term of office initiated a program for tuberculosis control, setting the pace for subsequent developments in this field. Dr. Murphy received the honorary degree of LL.D. from both Dalhousie and St. Francis Xavier universities. He was a former editor-in-chief of the *Nova Scotia Medical Bulletin* and he devoted a great deal of his free time to writing. His book, *Wood, Hay and Stubble*, was published in Anti-

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gonish in 1956. He was a Fellow of the Royal College of Surgeons of Canada and the American College of Surgeons, of which he was at one time Regent. In 1956 Dr. Murphy was made a senior member of the Canadian Medical Association.

He is survived by his widow and two sons, Dr. Arthur L. Murphy of Halifax, and Dr. George H. Murphy of Winchester, Virginia.

DR. JOHN HOWARD HOLBROOK

AN APPRECIATION

In the death on March 14 last of Dr. John Howard Holbrook, 82, retired medical superintendent of the Mountain Sanatorium at Hamilton, the Canadian medical profession lost a great leader in the fight against tuberculosis and an esteemed member of its councils.

In his 37 years at the Sanatorium, Dr. Holbrook had seen that institution grow from a few tents on the brow of the escarpment overlooking Hamilton into a great institution comprising many modern pavilions, its own farm, and the best that was to be had in staff and equipment. Dr. Holbrook's vision, his talent for organizing and administering, and above all his tremendous capacity for imparting his enthusiasm to all with whom he worked, were responsible for the Mountain Sanatorium's developing into the largest institution in the British Commonwealth for the treatment of tuberculosis.

Under the sponsorship and governing direction of the Hamilton Health Association, a group of citizens devoted to public service, the Mountain Sanatorium has always enjoyed a community support without which its success would have been impossible. The man responsible for enlisting, fostering and using to best advantage that support was Dr. Holbrook. Patrons of the Sanatorium through the years have given without stint both of their time and money toward furthering Dr. Holbrook's labour of love. The Mountain Sanatorium stands today a living memorial to Dr. Holbrook and his vision.

Born on a farm in Southern Ontario, John Howard Holbrook started out in life as a school teacher. But the call to medicine was not to be denied. As soon as his savings allowed, he enrolled in the University of Toronto's Faculty of Medicine and proceeded to his degree.

The opportunity for what was to be Dr. Holbrook's life work came in 1908, when he accepted the superintendency of the little 26-bed hospital where a few Hamilton citizens were arming to fight the scourge of tuberculosis. From that point, he never stopped. Even in retirement he sought out every chance to carry on the battle, now so nearly won.

If one were to search Dr. Holbrook's personality for the key to his success, it would most likely be found in the Kipling lines: "If you can walk with kings, nor lose the common touch." For it was Dr. Holbrook's "common touch" which commanded in his associates their confidence, their loyalty and their trust.

In later years, when honour upon honour was showered upon him, Howard Holbrook never lost in any way the wholesome simplicity and sincerity of the farm boy—the lad whose vision and courage and optimism were to play so great a part in the profession's unceasing battle against disease.

FORTHCOMING MEETINGS

CANADA

AMERICAN ACADEMY OF DENTAL MEDICINE, 12th Annual Meeting, Montreal, Que. (Dr. Louis J. Rosen, Convention Chairman, 3465 Côte des Neiges Road, Montreal, Que.) May 28-31, 1958.

CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES (Canadian Physiological Society, Pharmacological Society of Canada, Canadian Association of Anatomists, Canadian Biochemical Society), First Annual Meeting, Kingston, Ont. (Dr. E. H. Bensley, Honorary Secretary of the Board, Canadian Federation of Biological Societies, Montreal General Hospital, 1650 Cedar Avenue, Montreal 25, P.Q.) June 7-11, 1958.

CANADIAN OTOLARYNGOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OTOLARYNGOLOGIE), Annual Meeting, Halifax, N.S. (Dr. Donald M. MacRae, 324 Spring Garden Road, Halifax, N.S.) June 9-11, 1958.

CANADIAN TUBERCULOSIS ASSOCIATION, 58th Annual Meeting, Quebec City, P.Q. (Dr. G. J. Wherrett, Executive Secretary, Canadian Tuberculosis Association, 265 Elgin St., Ottawa 4, Ont.) June 9-12, 1958.

CANADIAN OPHTHALMOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OPHTALMOLOGIE), 21st Annual Meeting, Halifax, N.S. (Dr. R. G. C. Kelly, Secretary, 90 St. Clair Ave. West, Toronto 7, Ont.) June 12-14, 1958.

CANADIAN ASSOCIATION OF PLASTIC SURGEONS, Annual Meeting, Toronto, Ont. (Dr. D. C. Robertson, Medical Arts Bldg., 170 St. George St., Toronto 5, Ont.) June 12-14, 1958.

CANADIAN NEUROLOGICAL SOCIETY, 10th Annual Meeting, Toronto, Ont. (Dr. J. L. Silversides, Secretary-Treasurer, Suite 321, Toronto Western Hospital, Toronto.) June 12-14, 1958.

THIRD CANADIAN CANCER RESEARCH CONFERENCE, Honey Harbour, Ont. (Dr. Robert L. Noble, Medical Research Laboratory, University of Western Ontario, London, Ont.) June 15-19, 1958.

CANADIAN MEDICAL ASSOCIATION, 91st Annual Meeting, Halifax, Nova Scotia. (Dr. A. D. Kelly, General Secretary, The Canadian Medical Association, 150 St. George Street, Toronto 5, Ont.) June 16-20, 1958.

CANADIAN RHEUMATISM ASSOCIATION (SOCIÉTÉ CANADIENNE DE RHUMATOLOGIE), Annual Meeting, Vancouver, B.C. (Dr. de Guise Vaillancourt, Secretary, Canadian Rheumatism Association, Hôtel-Dieu Hospital, Montreal 18, Que.) June 18, 1958.

CANADIAN DERMATOLOGICAL ASSOCIATION, Annual Meeting, Halifax, N.S. (Dr. Gibson E. Craig, Secretary, Suite 6, 1390 Sherbrooke St. West, Montreal 25, Que.) June 19-21, 1958.

CANADIAN PSYCHIATRIC ASSOCIATION, Annual Meeting, Halifax, Nova Scotia. (Dr. Charles Roberts, P.O. Box 6034, Montreal, Que.) June 20-21, 1958.

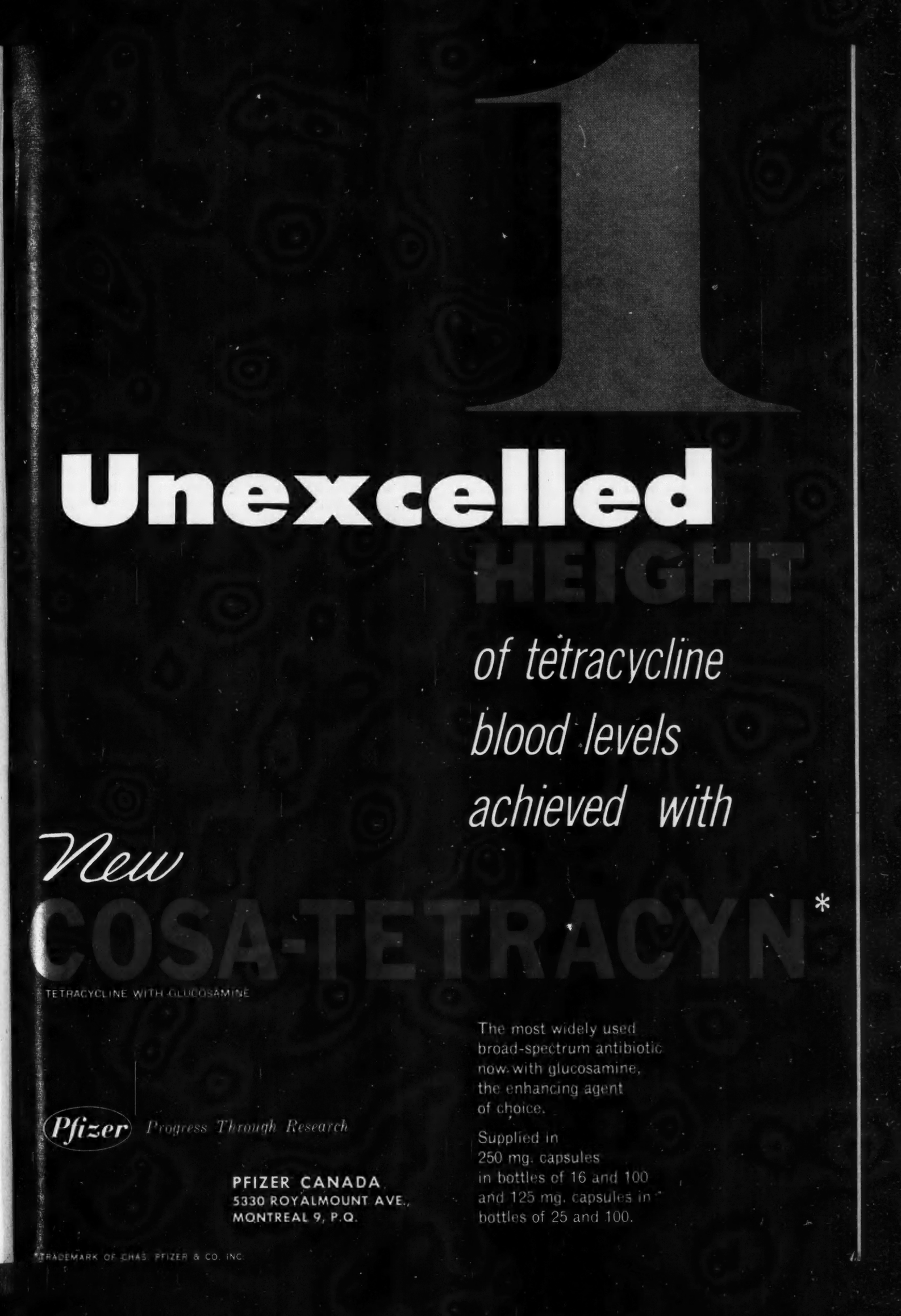
INTERNATIONAL FERTILITY ASSOCIATION, Windsor Hotel, Montreal, Que. (Dr. Walter W. Williams, 20 Magnolia Terrace, Springfield 8, Mass., U.S.A.) June 20-22, 1958.

INTERNATIONAL FEDERATION OF GYNÆCOLOGY AND OBSTETRICS, 2nd Congress, Montreal, P.Q. (Professor Léon Gérin-Lajoie, Suite 313, 1414 Drummond Street, Montreal, P.Q.) June 22-28, 1958.

10TH INTERNATIONAL CONGRESS OF GENETICS, Montreal, P.Q. (Mr. J. W. Boyes, General Secretary, 10th International Congress of Genetics, McGill University, Montreal, P.Q.) August 20-27, 1958.

UNITED STATES

INTERNATIONAL SOCIETY OF GASTROENTEROLOGY, 3rd World Congress, Washington, D.C. (Dr. H. M. Pollard, University Hospital, Ann Arbor, Michigan.) May 25-29, 1958.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PROVINCIAL NEWS

BRITISH COLUMBIA

The late session of the British Columbia Legislature has been one of great interest to the medical profession of this province, and indeed to the whole profession in Canada. Two items are of special interest: first, certain amendments to the Naturopathic Act, and second, some legislation that was designed to make it legal for dental technicians to make plates for people desiring them, without the latter having to consult a dentist and have the plates ordered by him, as the Dental Act prescribes up to the present.

First, as regards the naturopaths. Until now, it was the law that any one wishing to practise naturopathy in B.C. was required to pass examinations in basic subjects—anatomy, physiology, pathology and so on—set by a Board appointed by the University of British Columbia. This Board had, apparently, not been called on to function very often. It is possible that this was because would-be naturopath practitioners were rather afraid that they might not be able to pass the tests. In any case, the Government, through the Attorney-General, or the Minister of Health and Welfare, introduced a measure abolishing the Board and giving the naturopaths the right to set their own examinations and decide for themselves the fitness or otherwise of those applying to practise; hence they are given complete autonomy, and equal rights with the medical profession.

The medical profession regards this as a very retrograde step, and as a menace to public health in British Columbia. Nor are they alone in taking this view. The daily press has spoken in no uncertain terms, opposing this legislation. To quote from an outstanding editorial in the Vancouver Daily Province: "This bill would give the naturopaths, trained at purely commercial schools, virtually the same footing as the doctors of medicine, rigorously trained at the universities. There is no school of naturopathy in Canada. Ironically, all the naturopaths here were trained in the United States—but, of those same states, a considerable number who used to recognize naturopathy now no longer permit its practice; there are today only a handful of the 48 in which it survives."

The Vancouver Board of Trade, also, has sent a statement to the College of Physicians and Surgeons in which it states that, after careful survey, it disapproves entirely of the legislation, and considers that the Government has failed in its responsibility to guard the public in matters of health. Other responsible public bodies have also protested.

As regards the dental technicians, a bill giving them their demands reached the third reading, but this has been held up, for study by a committee of the House, and will be reported on later. This would appear to us to be another backward step, and not in the public interest, that untrained men should practise dentistry, for this is what this would mean. As a matter of fact, we understand that the majority of dental technicians are not in favour of the plan at all.

For a good many years, the medical profession of B.C. has been looking after old-age pensioners and indigent people whose means do not enable them to pay for medical service or medicines, under a contract with the provincial government, which has paid a per capita sum into the Fund, which is controlled by the medical profession and is known as the Social Assistance Medical Services (S.A.M.S. for short). This money is paid out on the receipt of accounts, which are properly assessed by the Medical Department. The accounts are based on our regular schedule of fees. The sum available has never been adequate to pay these bills in full, and in the past two or three years not much more than 50% of these legitimate bills has been paid—though the public, we believe, thinks it is a very good deal for the medical profession. In addition to this objectionable feature, there is also the fact that there is a good deal of abuse. Very often the relations and children of these pensioners demand unnecessary and extra attention, without themselves contributing in any way, though many of them are quite well-to-do.

For the past two or three years, the profession has been trying to get amelioration of these conditions. In the first place, it feels that the amount paid to doctors should be at least 60% of the amount due—even at this we are contributing 40% of the cost, a thing not done by any other department of society except the legal profession, which has been very generous in providing legal aid for people who cannot afford it.

Recently the B.C. Division of the C.M.A. has issued a statement to the Government to the effect that the profession will not renew their contract with that body unless these demands are met. This after months and months of attempts to negotiate, and flat refusals on the part of the Government. These people will still be looked after by the medical men but on their own terms, either as charity or through bills where it is felt that payment can be made by or for those concerned.

The Government has appointed a committee to meet the profession, and matters are in abeyance.

A record $241,000 was raised last year by the B.C. Tuberculosis Society through the sale of Christmas seals. The province is covered completely by these sales, and practically every centre last year increased its sales markedly.

The B.C. Alcoholism Foundation is extremely active —582 new cases have been treated in the last ten months, and 114 patients admitted for treatment.

Attorney-General Bonner states that groups studying narcotic addiction and alcoholism will get more money if they need it. Their budgets had been heavily cut, but he has promised to review their expenditures.

The Annual Meeting of the General Practitioners' Section of the B.C. Division was held at Harrison Hot Springs Hotel on March 3, and was very successful. An interesting feature was the paying of especial honour to Dr. E. C. Hart of Victoria, as the oldest active medical practitioner in British Columbia.

Dr. Hart came to B.C. in 1897, at a time when Victoria was considerably bigger than Vancouver, which had a population of 12,000 and was just beginning to recover from its destruction by fire in 1886. He has been coroner of Victoria for about half a century, and is regarded as outstanding in this capacity.

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Legislation to permit an agreement for a joint B.C.-Federal scheme of health insurance was introduced in the recent session of the Legislature.

It is proposed that the present year's delay before a person coming into B.C. may obtain benefits under B.C.H.I.S. will be reduced and ultimately wiped out.

At the annual meeting of the G. F. Strong Rehabilitation Centre this week, the President, Mr. Gordon Southam, reported that a seven-storey addition to the centre is planned, and work will start this fall.

The centre, which came into being some years ago as a result of the efforts of the late Dr. Strong and the Kinsmen's Club, has developed beyond all expectations. Its original aim was to provide for polio cases and cerebral palsy, but the new addition will provide services for the patients of the Canadian Arthritis and Rheumatism Society, and of the Cerebral Palsy Association of Greater Vancouver, as well as increasing the facilities for the work of the centre itself.

Mr. Gordon Southam was re-elected President.

J. H. MACDERMOT

MANITOBA

The Manitoba Cancer Treatment and Research Foundation has been established under a provincial Act to carry on the work of the late Manitoba Cancer Relief and Research Institute. The Foundation will provide diagnostic and radiotherapeutic services, while the Society will concern itself with raising of funds, lay education and patient welfare.

The Foundation comprises the Minister of Health and Public Welfare and nine members including Dr. M. R. MacCharles and Dr. C. W. Burns. The senior officers are: Executive, Dr. R. J. Walton; Senior Physicist and Director of Radiation Laboratories, P. A. Macdonald, Ph.D.; Comptroller, Mr. J. L. Steen. The address of the Foundation is 700 Bannatyne Avenue, Winnipeg 3.

Dr. Alexander Brunschwig, professor of clinical surgery at Cornell University School of Medicine, New York, and vice-president of the International College of Surgeons, had two busy days in Winnipeg on March 6 and 7. Invited by the University of Manitoba and the Canadian Chapter of the International College of Surgeons, he spoke in the medical college on pancreatic tumours, and at a luncheon meeting of the Winnipeg General Hospital on surgical problems arising when radiation therapy has failed to control cancer of the cervix. On the evening of March 7, he appeared before a crowded meeting of the Winnipeg Medical Society to give his impressions of a recent visit to Moscow and Leningrad, supplemented by numerous slides. He thought that Russian medical work in those two centres was on a par with that in the United States and Canada.

Dr. Henry Hildebrand (M.D. Man. '56), who has been practising at Teulon, Manitoba, will sail from New York in August for Belgium where he will take courses in tropical medicine and French for a year. He and his wife and two sons will then proceed to the Belgian Congo, where he will have a medical mission.

Dr. Stanley Rische has joined the radiotherapy department of the Winnipeg General Hospital. He received his undergraduate training in Middlesex Hospital, graduated M.D. in general medicine and pathology while still in the R.A.F., and obtained his diploma in medical radiotherapy under Professor Windeyer of Middlesex Hospital.

Tenders have been called for a three-storey, 88-foot addition to the psychiatric department of the Winnipeg General Hospital. The 54-bed addition will be on the north side of the present building and will be used as a diagnostic clinic for early acute cases of mental illness.

The President of Manitoba University has announced three appointments to the Faculty of Dentistry which will admit its first class in September. Dr. Harold W. Hart is to be head of the department of prosthodontics. He is retired chief instructor in the Royal Canadian Dental Corps training school. Dr. Brass will be head of the department of operative dentistry. At present he is associate professor of operative dentistry, University of Alberta. Dr. Sinclair-Hall will be lecturer in anatomy. He obtained his M.D. from the University of Manitoba in 1930 and Fellowship in the Royal College of Surgeons, Edinburgh. The Dental College will be erected to the west of the Medical College.

ROSS MITCHELL

NEWFOUNDLAND

"THE STATE AND MEDICINE"

On Feb. 20, almost a hundred members and guests of the St. John's Clinical Society turned out to discuss the theme "The State and Medicine". The principal speakers were Dr. C. B. Stewart, Dean of Medicine at Dalhousie University, Dr. L. A. Miller, Deputy Minister of Health of Newfoundland, and Dr. G. M. Brownrigg. The following account of the proceedings is taken from the minutes of the Secretary, Dr. J. B. Ross.

"Dr. Miller was the opening speaker. He remarked that objective appraisal of the problem was hardly possible but should be attempted. Difficulties that had to be faced in the relationship of the State and medicine were: that the doctor's training is highly individualistic—medical students do not know enough about community life; secondly, that there is a savage jealousy of the doctor-patient relationship; thirdly, that nobody wants to be sick, so they do not want to pay for sickness. Democratic process encourages the government to provide what the people need, and indeed political parties are often obliged against their will to provide services. The question was—where should the funds come from for the health of the nation? Should it be in the open market or was it the community's responsibility? In the past, state-sponsored medicine had been responsible for the reduction of killing illnesses—for instance, diphtheria and tuberculosis. It was felt by many that this was the best form of medicine.

(Continued on page 744)

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"Dr. Stewart was the next speaker. He said that the problem was to provide for the people of Canada a comprehensive health service maintaining the high standard of medicine as in the past, which would contribute to the improvement of medicine and yet continue to recruit into the profession the very best of people. Dr. Stewart quoted figures showing that it costs $2000 per year to maintain a medical student at the present time as opposed to $287 in the 1922-23 period. The State must therefore contribute more to the upkeep of medical education. However, there must be full academic freedom. The universities must select their students. In some places there has been some interference in the freedom of the universities. Dr. Stewart was concerned with the fall in the standard of recruits to medicine and the falling number of applications in the schools. He felt this was due to the length of education at the present time and the fact that doctors generally look and speak gloomily of State medicine, which seems imminent. Dr. Stewart explained how he had felt critical of a committee of the C.M.A. which had declared that it felt that doctors were not qualified to prepare a health plan. Government should prepare a plan, they said, and the profession would be in a position to criticize. Dr. Stewart felt that the profession should come forward with a definite plan.

"Dr. Brownrigg declared his pessimistic outlook on the present situation. The bewildering speed of changes, he declared, confuses us and entitles us to become confused. We could take heart, as there seemed to be equal confusion in Ottawa. He declared that the lack of discipline in democracy in general may lead to a loss of democracy, and quoted from Durant's 'History of Greece' to the effect that no great nation is ever conquered until it defeats itself. He saw men divided into two classes—those who sought achievement, prestige, and wealth, and those who sought security and handouts. The first class accepted a discipline and a general upward striving. He put the profession in that class. Security-seekers, he felt, were the great masses. He felt that the fate of democracy was to have to submit to the rule of the wishes of the undisciplined masses. Without the responsible hand of an upper house, democracy must fail. With the tremendous impact of science on medicine, the hospital system has grown tremendously and so have the costs of such a system. Only government has the means of wealth, but government can only get the money from the people. If a sense of responsibility is given to citizens the plans may succeed. Additional taxes will be necessary. Deterrents may prove the answer to giving responsibility."

After the formal presentations by the three members of the panel, the meeting was thrown open to the house for questions and comment. Panel and audience put forth their views on many matters, such as the desirable aspects of medical practice which should be maintained, the doctor-patient relationship, government interference in universities, methods of financing medical care to lower-income groups, the importance of self-discipline within the profession, and relationships between profession and government, etc.

A. J. NEARY

BOOK REVIEWS

MODERN TREATMENT YEARBOOK 1957. Edited by Sir Cecil Wakeley, King's College Hospital, London. 312 pp. Illust. Baillière, Tindall and Cox, London; The Macmillan Company of Canada Limited, Toronto, 1957. $4.25.

The 32 chapters making up this book were contributed by eminent authors, each expert in a particular field of medicine. The chapters cover a multitude of subjects of interest particularly to the general practitioner and they are arranged in random order so that you will find "The Management of Colostomies" immediately following "The Treatment of Bites and Stings". The chapters cover not only the latest treatment but also give accounts of etiology and pathology, as well as a well rounded out discussion of clinical aspects of the subject.

As with most volumes of this kind which cover such a broad field, the discussions are of necessity quite short, but are adequate to refresh one's memory and bring it up to date. Usually, the author presents his views on the latest method of treatment without discussing alternative methods, and in many chapters no references are listed. The presentation of the subject matter makes interesting and easy reading. The photographic plates are arranged in a separate section near the centre of the book to make them readily accessible. These are good reproductions and they clearly illustrate the conditions or apparatus under discussion.

It is not often that we see surgical and medical subjects discussed side by side in a book, and yet the practitioner is confronted with this very situation every day. This book combines very interesting and enjoyable reading and should serve as a handy guide for the general practitioner for whom it was intended.

BRITISH PHARMACOPŒIA 1958. 1012 pp. Published for the General Medical Council by the Pharmaceutical Press, London; The Jefferson Press, Toronto, 1958. $12.50.

The new edition of the *British Pharmacopœia* appears approximately five years after the last edition; however, an addendum to the latter was published in 1955. It is gratifying to note that in the introduction to the present edition, credit is paid to the arduous work of the Canadian corresponding members to the various Pharmacopœial committees. Consultation for this edition has been on a very wide basis indeed throughout the entire Commonwealth. New monographs on drugs cover a wide range of synthetic drugs, antibiotics, hormones and biologicals together with preparations such as injections and tablets. Various standards and tests have been revised and new monographs added on certain mixed antigens. For the first time, the Pharmacopœia includes monographs on radioactive chemicals (radioiodine and radiophosphorus). Doses are now expressed in the metric system only, except for those substances and preparations still commonly prescribed in Britain in the imperial system. It may well be that in the next edition the imperial system of dosage will have been abandoned. Deletions include some old favourites of traditional medicine such as the aromatic spirit of ammonia, the compound powder of rhubarb and the liquid extract of senna. Some other old standbys such as tincture of digitalis and amyl nitrite, and older sulfonamides such as sulfathiazole, have been

weeded out. Changes in title are few; tetanus toxoid has become tetanus vaccine; diphtheria prophylactic has become diphtheria vaccine. A list shows the titles of those monographs in which the B.P. name differs widely from the names in the *International Pharmacopœia.*

NEW AND NONOFFICIAL DRUGS 1958. Evaluated by the A.M.A. Council on Drugs. 645 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1958.

The latest edition of *New and Nonofficial Drugs* contains monographs on 48 new drugs evaluated and described in the columns of the *J. A. M. A.* Nine monographs have been omitted from the present edition on the grounds that the drugs described are well known through their inclusion in the *U.S. Pharmacopœia* or the *National Formulary* or elsewhere. The policy of the work remains unchanged, namely to describe drugs which the Council on Drugs of the American Medical Association has evaluated, and which have not yet found their way into standard works with editions at much longer intervals.

AMERICAN DRUG INDEX 1958. Charles O. Wilson, University of Texas, and Tony Everett Jones, University of Colorado. 716 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1958. $5.00.

Once more we welcome this invaluable little list of drugs and preparations. It is quite the best publication for finding one's way among the morass of proprietary and non-proprietary names. It is heartily recommended as a reference work for all who have to do with drugs.

PHYSIKALISCHE GRUNDLAGEN DER ROENTGEN-DIAGNOSTIK (Physical Bases of Radiological Diagnosis). P. G. Spiegler, London, England. 94 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1957. $4.30.

In this small volume, Dr. Spiegler, who for many years has lived in England, has undertaken the desirable task of translating the physics of radiation into the field of roentgen diagnosis. In six well-illustrated chapters the author discusses the effect of the roentgen rays upon the contrast of the x-ray image, the volume of the rays and its relation to the rayed object, their effect upon the resulting photographic image, the physics of the x-ray exposure, the surface and the depth dose and its relation to the contrast of the roentgen image, the geometric factors as related to the enlargement technique, the value of the high kV technique versus standard kV technique, calibration of x-ray equipment for output, contrast and kilovoltage and other related subjects. The object of obtaining a harmonious roentgen image is discussed at length in Chapter 4. The last two chapters deal with secondary radiation and protection and with the interpretation and the meaning of the roentgen shadow. Some of the data presented in these two chapters were obtained in collaboration with Mr. B. E. Keane, physicist to the Royal Sussex Hospital, Brighton, England.

The writing of this book was encouraged by Prof. Mayneord of London and many physicists and radiologists in Great Britain, Germany and Holland, who provided the author with illustrations used in the text.

This book provides one with very interesting, though perhaps not the most easy reading. It opens a new vista of the foundations upon which the roentgen image is created. As Professor Schinz states in his introduction to Dr. Spiegler's book: "The roentgen image is an image of absorption, partly that of a shadow, and partly that of transmission of light, but mostly it is a combination of both." Dr. Spiegler's book makes the roentgen image understandable.

There is an up-to-date list of references which adds to the value of this publication.

LES CAHIERS DE L'HOTEL-DIEU DE QUEBEC 1956. Chroniques médico-hospitalières. 278 pp. Illust. L'Hôtel-Dieu de Québec, Quebec City, 1957.

This beautifully presented annual record of the work of Quebec's chief hospital, l'Hôtel-Dieu de Québec, is now in its tenth year. The major portion of the volume is as usual made up of scientific contributions from the staff of the hospital. Some of these have been printed in such periodicals as the *Canadian Medical Association Journal* and *Laval Médical;* others appear for the first time. As usual, a wide range of specialties is covered and most of the articles are in French. The remainder of the volume contains a considerable amount of information on the general and specialized courses of instruction held at the Hôtel-Dieu, a list of staff, and an historical article on some of those intrepid religious without whom the Hôtel-Dieu could never have existed.

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BOOK REVIEWS

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SEKRETIONSSTUDIEN AM PANKREAS: Experimentelle und anatomische Pathologie (Studies of Pancreatic Secretion: Experimental and Anatomical Pathology). Series—Normal and Pathological Anatomy, No. 1; Series editors, W. Bargmann and W. Doerr, Kiel. No. 1: Volker Becker, Kiel. 119 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1957. $7.00 (series subscription rate $5.60).

This is the first volume of a new series of "Monographs on normal and pathological anatomy", edited by Dr. Bargmann and Dr. Doerr, Professors of Anatomy and Pathological Anatomy at the University of Kiel, Germany. The present volume is an attempt by a morphologist to correlate the microscopic appearance of the pancreas with its secretory function. Material from animal experiments is used to provide a basis for interpretation of histological changes in human autopsy material. The author proposes an interesting and, from the histological point of view, well-documented theory concerning the mechanism of pancreatic exocrine secretion. He attributes the secretion of enzymes and protein components to the acinar cells, and the secretion of water and electrolytes to the tubular epithelial elements. Pathological pictures of pancreatic dysfunction are then interpreted in the light of this theory. A fairly complete list of publications concerning pancreatic function and pathology is a useful appendix to this well-illustrated publication.

TEN MILLION AND ONE: Neurological Disability as a National Problem (Arden House Conference, sponsored by The National Health Council). 102 pp. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1957. $3.50.

This brief book represents the results of a conference sponsored by the National Health Council of the United States which was concerned with the over-all problems of neurological disability.

Expert opinions from a wide variety of sources were requested, in order to arrive at a co-operative approach to the problem of diagnosis, treatment, management, and vocational placement of some ten million people in the United States affected with neurological disabilities of various types. The magnitude of the problem is emphasized and the need for combined technical, professional, scientific and community resources in the solution of this problem is stressed.

The book would be of interest to anyone concerned with the numerous facets of neurological disability from the standpoint of its present problems and future management.

DRUGS AND THE MIND. Robert S. de Ropp, University of London. 310 pp. St. Martin's Press, New York; The Macmillan Company of Canada Limited, Toronto, 1957. $4.50.

This book is presented primarily for the layman and non-medical scientist. It encompasses the historical and scientific background in the use of various drugs and medications that influence the working of the mind. The vivid descriptions presented and the numerous quotations given are particularly fascinating and would be worthwhile reading for all, including the medical profession.

Comprehensive references are made to the use of mescaline and marihuana by Aldous Huxley, Havelock Ellis, De Quincey, and Baudelaire. Some of their vivid experiences and descriptions form classical literary masterpieces. Further chapters deal

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BOOK REVIEWS

(Continued from page 49)

with some of the newer chemical discoveries related to the function of the mind. These include the use of the now overly popular ataractic and analeptic drugs as well as the induction of transient drug psychosis. The numerous possibilities in this field of chemopsychiatry are considered in some detail.

In general this book provides a most entertaining dramatized description of this current and fascinating subject.

CLINICAL APPLICATIONS OF SUGGESTION AND HYPNOSIS. William T. Heron, University of Minnesota, Minneapolis. 165 pp. 3rd ed. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1957. $4.25.

This is a general review by a psychologist of hypnosis clinically practised. It is simply and clearly written and easily understood. Throughout, the impression is given that hypnosis is a professional technique and one to be used only by skilled, responsible professional men.

It is, perhaps, somewhat unfortunate that the book seems to be aimed at the dentist rather than the doctor. On the other hand, the lucidity of the text recommends itself strongly to the person who knows nothing of hypnosis and wishes to be informed. Very clear instructions are given as regards technique.

ORTHODONTICS: Principles and Prevention. J. A. Salzmann, Mount Sinai Hospital, New York. 381 pp. Illust. J. B. Lippincott Company, Philadelphia and Montreal, 1957. $13.00.

This work contains a discussion of the application of orthodontics and preventive (prophylactic) orthodontics in general practice and in public health programs. Hence it is of interest to the medical practitioner, especially the pædiatrician. The chapter on assessment of growth and development includes practical procedures and growth standards in current use, while the material on the organization of bone and the assessment of skeletal development also includes practical standards which may be applied clinically.

Prenatal and postnatal skull growth are described from the functional point of view as they express themselves in normal and abnormal growth. Craniofacial growth is discussed in relation to the development of dental occlusion.

The various forms of dental occlusion, the physiology of the tempo-

(Continued on page 54)

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BOOK REVIEWS

(Continued from page 50)

romandibular joint and the muscles of mastication are discussed in the chapter on the stomatognathic system.

In the chapters on the development of the dentition, standards of eruption, and anomalies of tooth formation and eruption will be found material of interest to both student and graduate, while in the chapter on ontogenetic development of the occlusion of the teeth are outlined the changes in the dental arches from the beginning of tooth eruption of the deciduous teeth to the completion of eruption of all of the permanent dentition.

This book is useful as a reference work.

A companion volume on orthodontics, practice and teachnique, is available to those who wish to delve more deeply into the practical application of the principles outlined above in the maintenance, preservation and restoration of normal occlusion.

DIGITALIS. Compiled and edited by E. Grey Dimond, Department of Medicine, University of Kansas Medical Center, Kansas City, Kansas. 255 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1957. $7.75.

This volume consists of a series of papers given at the University of Kansas in 1956, in a symposium on digitalis. These papers were supplemented for publication by one on the historical aspects by Dr. Major and by two on recent pharmacological actions. Of particular interest is Bing's description of our present knowledge of muscle contraction and the effect of glycosides on it. Batterman and Sodeman contribute two valuable papers on the clinical use of the drug. The toxic effects on the atrium are also described. An informative panel discussion closes the volume.

This is not to be regarded as a complete text on the employment of digitalis, but rather as a presentation of recent viewpoints and data which it might be difficult to assemble otherwise. It should be studied, at least in part, by every practitioner, but will be stimulating particularly to the internist and cardiologist.

CHRONIC ILLNESS IN THE UNITED STATES: Vol. I, PREVENTION OF CHRONIC ILLNESS. Commission on Chronic Illness, June 1949-June 1956. 338 pp. Harvard University Press, Cambridge, Mass.; Oxford University Press, London, 1957. $6.60.

This volume is the first to appear in a series of four, to contain the complete findings and recommendations of a voluntary (U.S.) Commission on Chronic Illness, after a seven-year study of the problem (1949-56). Many national (medical, social, welfare, industrial, etc.) organizations aided the commission in its work of gathering, formulating and disseminating information on all the facets of chronic illness. Dr. Leonard Mayo acted as commission chairman.

Volume I, under review here, is restricted to a detailed study and presentation of the data obtained relating to the preventive aspects of chronic disease. Primary prevention methods (known methods of averting a pathological process) and secondary prevention, comprising methods of early diagnosis via screening procedures, etc., and therapy directed to avoiding progressive disability, are detailed and thoroughly discussed. In fact, the commission has gathered and documented in this

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BOOK REVIEWS

(Continued from page 54)

volume about all that is currently known in the above respects. Seventeen chapters are devoted to summaries of information on prevention of selected chronic diseases and contributory factors.

The expressed aim of the commission is stated to be an attempt, through dissemination of the accumulated knowledge, to modify the prevalent attitude of society that chronic illness is hopeless. All will agree that the basic approach to chronic illness must be preventive if the problem of such disease is ever to be controlled. However, the report points out and acknowledges the wide gaps in our medical knowledge regarding the etiology and unavailability of specific early diagnostic tests for many of the commonest chronic diseases. Coronary atherosclerotic heart disease, of still undetermined etiology, is said to account for about one-half of the male deaths in the U.S.A. today. The commission report tries to point out areas of probable fruitful research directed towards elucidating these problems and further advance primary prevention of chronic illness. Nevertheless it is felt that the full application of the preventive knowledge presented in this volume would markedly reduce the burden of chronic disease. This "full application" will depend on individual and public enlightenment and education via dissemination of information, and this is one of the major responsibilities the commission has accepted.

This volume, containing the assembled results of much factual research into the factors governing the prevention of chronic illness and disability, is highly recommended as desirable reading and as a reference manual for all medical, social, welfare and research workers.

THE DOCTOR EYES THE POOR READER. Delwyn G. Schubert, Associate Professor of Education, Los Angeles State College of Applied Arts and Sciences, Los Angeles, California. 101 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1957. $4.00.

The physician should be prepared to recognize children with reading difficulties and should be able to advise parents on what can be done for such children. This book attempts to tell the physician how to diagnose a case of reading difficulty, what are the likely causes, and what forms of treatment may be helpful. In bringing to the attention of physicians the fact that a problem does exist it will perform a useful service.

MEDICAL NEWS *in brief*

(Continued from page 716)

TREATMENT OF CERVICAL SYNDROME BY TRACTION

In a recent issue of *Nederlands Tijdschrift voor Geneeskunde* (102: 5, 1958) a Dutch physician describes the treatment of 143 patients complaining of the cervical syndrome by head traction once a day for 15 minutes with a Glisson sling to which a 15-kg. weight was attached, with the patient in the sitting position and as relaxed as possible. All these patients had suffered from their pain for more than three months and had had at least three months' unsuccessful

treatment with the usual drugs and physiotherapy. During the traction treatment, all other therapeutic measures were abandoned. After four days, 14% of the patients were definitely free from symptoms; after eight days 29% were freed, and after 12 days 47% were free from symptoms and another 11% significantly improved. Recurrence within one to two years was rare. Results were not correlated with sex or age, or with the relationship between the clinical picture and radiological picture.

DIAGNOSTIC APPLICATIONS OF RADIOACTIVE ISOTOPES

A manual entitled "Diagnostic Applications of Radioactive Isotopes" has recently been published by Nuclear-Chicago Corporation. This two-colour 24-page brochure describes procedures involved and instrumentation required for the nine most commonly used radioisotopes studies.

Included are procedures on the following applications: (1) evaluation of thyroid function using radioiodine; (2) studies of kidney function with radioactive Diodrast; (3) estimation of cardiac output with radioiodinated serum albumin; (4) evaluation of liver function with radioactive rose bengal; (5) blood plasma volume measurements using radioiodinated serum albumin; (6) measurement of red cell mass with radiochromium; (7) diagnosis of pernicious anæmia with radiocobalt vitamin B_{12}; (8) fat digestion and absorption with radioiodine labelled triolein; (9) scanning body areas for radioisotope concentrations. Address enquiries for copies to Nuclear-Chicago Corporation, 223 West Erie Street, Chicago 10, Illinois, U.S.A.

SYMPOSIUM ON BASAL GANGLIA SURGERY

A three-day symposium on "Basal Ganglia Surgery for Involuntary Movement Disorders" will be held at New York University-Bellevue Medical Center from Thursday, May 15, to Saturday, May 17. Dr. Irving S. Cooper, Professor of Research Surgery in the Department of Surgery of New York University Post-Graduate Medical School, is symposium chairman. Complimentary tickets for the meeting, the program, and hotel reservation blanks will be sent on request to Miss Dorothy P. Frome, Office of Public Relations, 550 First Avenue, New York 16, New York.

PERSONALITY IN OLD AGE

Interest in old people is looming larger all the time. It has now become commonplace to refer to medical progress in the light of the average lifespan. However, the centenarian, who used to be looked upon at worst as a freak of nature and at best as a medical curiosity, is now receiving the attention that a moderately frequent social phenomenon deserves. In the inventory of our knowledge of old age, not only were several gaps discovered, particularly with regard to simple

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MEDICAL NEWS *in brief*
(Continued from page 57)

physiological aging uncomplicated by disease, but many fallacies were revealed which were hitherto considered as well proven truths. Presumably the inadequacy of sampling in the past may account for both deficiencies.

General efficiency and intelligence which were believed to decrease with age may on the contrary increase in many respects. The part played by a college education is considered to be the main factor in the discrepancy formerly obtained on the intelligence tests between young and old people. A direct socio-economic consequence of revision of this concept should be a new attitude towards forced retirement and the wastage in manpower which it implies.

In a survey carried out for the purpose of establishing the personality pattern of healthy centenarians and those whom Gumpert refers to as "nimble nonagenarians", Flanders Dunbar (*J. Am. Geriatrics Soc.*, 5: 982, 1957), undertook the study of several elderly persons. Most of them reported "an extraordinary freedom from illness". In their behaviour in relation to stress, it was found that "they avoided some types of stress whenever possible, but . . . actually sought others". Among the forms of stress which they avoided was that of frustration. These people managed to escape conflict with authority. They strove to be their own boss without necessarily trying to rule others in the process. "They value independence and attempt to apply the principles of a democracy as a basis for cooperative and productive living." In their undertakings they are not possessed by the demon of ambition and are not perturbed if they do not reach the top rungs of the ladder. Being endowed with a sense of humour they are sociable and are not litigious, although they do not shun a fight when major issues are concerned. "They have a happy faculty of not worrying about things beyond their control . . . are extraordinarily active and rarely over-weight." The interviewers were impressed with their subjects' honesty, which nonetheless left room for some kidding.

Although these characteristics are probably inherited and not acquired, they still point to the importance of a well-balanced personality and a good adaptation.

STEROID AEROSOL IN ASTHMA

The control of cough in asthma is sometimes difficult. The tracheal mucosa is often irritable to the extent of reacting violently to the slightest stimulus. Peters and Henderson (*Proc. Staff Meet. Mayo Clin.*, 33: 57, 1958) have repeatedly tried the topical use of steroids in aerosol in order to take advantage of their anti-inflammatory property. However, it was not until they came across prednisolone phosphate that they were able to obtain a satisfactory solution. They have treated 11 patients with asthmatic bronchitis by means of prednisolone phosphate aerosol (0.5% solution) in conjunction with isopropylarterenol hydrochloride (Isuprel).

The results have been encouraging, and although they have not been as dramatic as with the parenteral use of steroids, side effects have been negligible. This form of therapy is considered worthy of further trial.

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MEDICAL NEWS *in brief*

(Continued from page 58)

ADULT SCURVY

Readers of this Journal have recently been made aware that scurvy can still be encountered in the child population of this country. A recent article from King's College Hospital Medical School, London, deals with the same problem in the adult population (R. H. Cutforth, *Lancet*, 1: 454, 1958). Eleven such patients were seen between 1951 and 1957 in the wards and outpatient departments of two London teaching hospitals. There were 10 men and one woman, and their ages ranged from 48 to 82 with an average of 65. Except for one patient who was married and was living with his wife, the remainder had a roughly comparable social background in that they were single, widowers or separated, and all were living alone. From a dietary point of view, all had had a deficient food intake mostly of the tea-and-toast variety except for two who had duodenal ulceration, one with chronic cholecystitis and one who was a "food crank". It is interesting to note that the commonest physical sign present in this series was small spontaneous bruises on the limbs. Bleeding of the gums, which receives so much emphasis in the clinical description of scurvy in most textbooks, was present in only one of these patients. Symptoms included pain in the limbs, anorexia, lethargy and stiffness of the legs, most of which cleared shortly after the onset of treatment. A relatively unknown sign of scurvy was observed in this small group consisting of psychological effects such as depression, resentment and lack of co-operation which soon gave way to a normal and cheerful disposition with treatment. With regard to the blood changes, it has been stated that the degree of anæmia is proportional to the amount of blood lost in the tissues; however, such a statement could not be confirmed in the present series since no correlation could be established between these two terms.

THIRD WORLD CONGRESS ON FERTILITY AND STERILITY

The Third World Congress on Fertility and Sterility, sponsored by the International Fertility Association, will be held in Amsterdam, Holland, from June 7 to 13, 1959.

The general outlines of the sections of the program will be as follows:

1. Female sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).

2. Male sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).

3. Basic research and/or animal reproduction.

4. Psychosexual problems.

Although any original report on some phase of fertility and infertility, either clinical or in the field of the basic sciences, will be considered, definite priority will be given to those papers concerning the following subjects:

1. Embryonic death (etiology, pathogenesis, placental structures

in relation to condition of fetus, functional problems and diagnosis of the embryonic and fetal death, and habitual abortion).

2. Hormonal factors and vitamins in fertility and sterility (ovulation and sterility, induction of ovulation, influence of thyroid, steroids, etc., on ovulation, influence and physicopathological significance of vitamins, hormones and spermatogenesis, vitamins and spermatogenesis).

3. Relative value of techniques for study of endocrine function in human sterility (study of œstrogen function, luteal function, adeno-hypophysis function, testicular biopsy value, study *in vitro* of fertilization of mammalian and human ova, use of radioisotopes in study of sexual function).

4. Biochemistry of spermatogenesis.

5. Psychosexual problems in sterility.

The official languages will be: English, French, German, and Spanish (with simultaneous translation).

Titles for papers should be sent not later than June 30, 1958, to both Dr. Alfonso Alvarez-Bravo, Avenida Horacio 1506, Mexico City 5, D.F., Mexico, chairman, and Prof. Dr. B. S. ten Berge, Academisch Ziekenhuis, Groningen, Holland, executive member of the Program Committee. For further information and registration apply to Dr. L. I. Swaab, Honorary Secretary, Third World Congress on Fertility and Sterility, Sint Agnietenstraat 4, Amsterdam-C., or to the nearest Wagons Lits/Cook office.

NEW MEDICAL DIRECTOR OF AMERICAN HEART ASSOCIATION

Dr. George E. Wakerlin has been appointed medical director of the American Heart Association as of April 1. He has been professor and head of the department of physiology of the University of Illinois College of Medicine, Chicago. Dr. Wakerlin replaces Dr. Ferris, who died last September.

NUTRITIONAL STATUS OF ALASKAN ESKIMOS

The nutrition of the Eskimo has intrigued specialists for some time, in view of the statements made that his race is relatively free from coronary attacks and the possibility that this might be associated with his unusual diet. The U.S. Public Health Service announces that a team of food and nutrition specialists is in Alaska working on the first large-scale study of the nutritional status of Alaskan Eskimos. The team will visit ten native villages and will examine and study approximately 1000 Eskimos, in order to find out how well the native diet meets nutritional requirements. A pilot study has already been made during the past two years by Dr. Christine Heller of the Arctic Health Research Center, who has lived among the villagers and recorded their daily food intake. After the current survey, the laboratory equipment and supplies will be turned over to the Research Center for continuing the job.

In infectious and allergic rhinitis and sinusitis

Biomydrin "is effective as an antibiotic in clearing the nose of pathogenic organisms and purulent secretions. In many cases, sterile cultures were obtained after a brief period of treatment."

Antibiotics & Chemotherapy 3:299 (March) 1953.

Improvement in 113 of 124 Patients*

Diagnosis	Number of patients	Improved
Chronic catarrhal rhinitis	11	11
Chronic allergic rhinitis	26	25
Right maxillary sinusitis	2	1
Chronic naso-pharyngeal catarrh	6	6
Chronic suppurative sinusitis	3	3
Coryza, Head cold, Catarrhal rhinitis	58	51
Influenza	2	1
Acute catarrh	4	3
Hypertrophic rhinitis	12	12
TOTAL	124	113 (91.1%)

*Eye, Ear, Nose and Throat Monthly 32:512 (Sept.) 1953.

The Biomydrin formula

THONZONIUM BROMIDE 0.05%. Synthesized in the Warner-Chilcott laboratories. Exceedingly potent antibacterial. Greatly enhances the antibiotic activity of neomycin and gramicidin. Reduces surface tension, facilitating spreading and penetrating. Mucolytic.

NEOMYCIN SULFATE 0.1%. Effective against gram-positive and gram-negative organisms.

GRAMICIDIN 0.005%. Effective against gram-positive organisms.

PHENYLEPHRINE HCl 0.25%. Widely preferred vasoconstrictor.

THONZYLAMINE HCl 1.0%. *Therapeutic concentration* of this effective antihistaminic aids in controlling local allergic manifestations.

- Prompt, prolonged shrinkage of nasal mucosa without secondary congestion.
- pH is 6.2 Isotonic and buffered.
- Does not interfere with ciliary activity.
- Spray covers larger area than could be reached by drops.

DOSAGE: Adults—2 or 3 sprays in each nostril; 4 or 5 times a day as needed, or as directed by physician. Children—1 or 2 sprays in each nostril; 4 or 5 times a day as needed, or as directed by physician.

BIOMYDRIN

WARNER-CHILCOTT
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